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# Science

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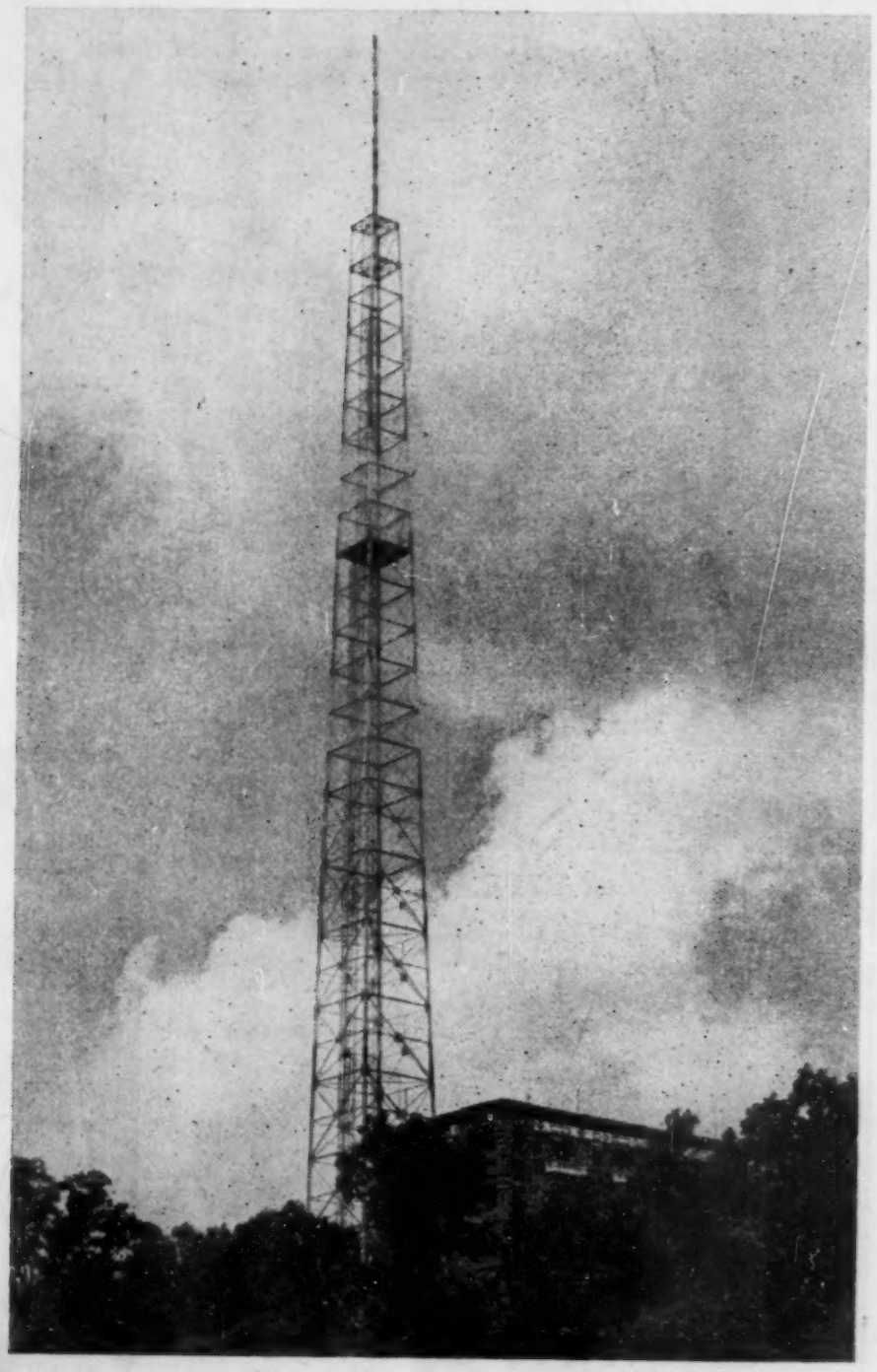

Television tower. (See *News and Notes.*)

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## A Survey of the Sciences

Richard C. Tolman

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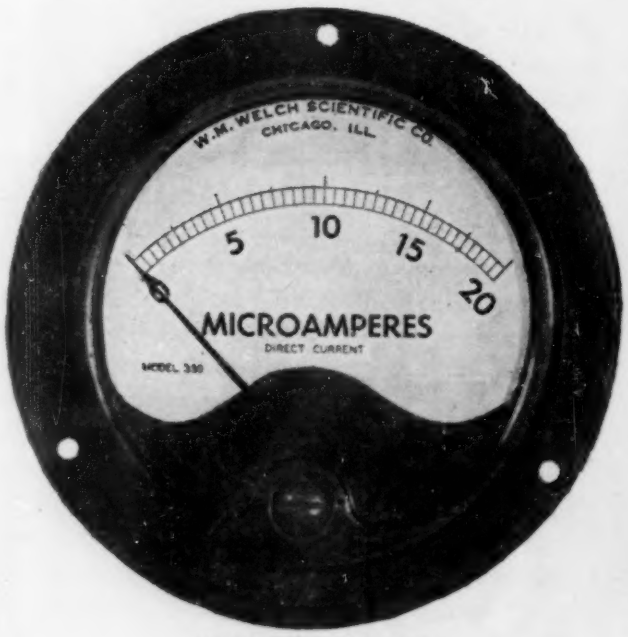


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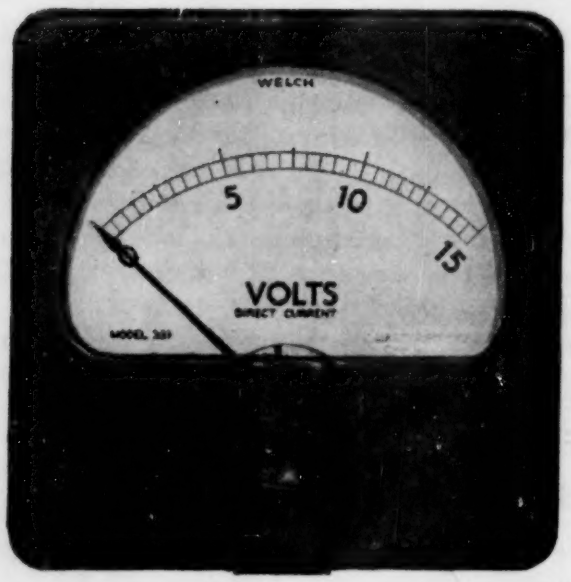


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# A Survey of the Sciences

**Richard C. Tolman**

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THE TITLE WHICH I HAVE CHOSEN FOR this address is a presumptuous one. In a brief half hour we must attempt a survey of the sciences, give some idea of their different natures, tell something about their present doings, and throw a look to their future. To find our way through this difficult task, we shall need some guiding principle. For this purpose let us regard the different sciences as arranged in a hierarchy, on a sort of ladder, in the order of their abstract character. This is a useful principle of arrangement for which we have long been indebted to the French philosopher, Auguste Comte, along with some other good things and some pompous bosh.

At the base of the ladder we place mathematics, the discipline which carries furthest the process of abstraction, by selecting—abstracting out—for study from the real world only the simplest and most general concepts such as those of order, number, and dimensionality. By taking into consideration further concepts abstracted out from the real world, such as those of matter, energy, and electricity, we come to the science of physics. By including the concept of different kinds of substance and of chemical change from one kind to another, we arrive at chemistry. By adding the concepts of a special kind of matter called living and of a special kind of behavior called mental, we come to biology and psychology. And, by including in our study more and more of the complexities of the actual world around us, we could pass on to social psychology, economics, and the social sciences in general. Let us now look at some of these sciences in the order named.

We start with mathematics—so-called Queen of the Sciences. For a mathematician this might mean Queen "over" the Sciences; you remember the dictum of Pythagoras, who said, "All things are number." But for a physicist, like myself, it cannot mean more than Queen "among" the Sciences. There are three things about mathematics of which I wish to speak: its simplicity and generality, its freedom of invention, and its logicality in accomplishment.

The simplicity and generality of mathematics reside in the simple and general character of the elements that it picks out for study. These are such things as order, number, magnitude, dimensionality, functional dependence, proximity, inclusion, and exclusion, which prove on examination to be quite simple and general notions. Thus, the idea of number is a simple and general one, as, for example, the simple three that characterizes these three fingers or the first three men in the front row, and the general three which characterizes all other collections of three objects. Mathematics is sometimes hard for you and me to understand, not because the mathematician chooses complicated things to talk about, but because he says such complicated things about them. As the study of mathematics becomes more profound, the elements selected for study may even tend to become simpler. Finally, they become meaningless p's and q's on a piece of paper which have no properties beyond those contained in the rules chosen for their manipulation, and no function except in testing the internal consistency, rather than the truth, of the results of such manipulation. It is at this stage that Bertrand Russell makes the humorous comment, "Mathematics may be defined as the subject in which we never know what we are talking about nor whether what we are saying is true."

The freedom of invention in mathematics lies in the liberty of the mathematician to create new elements for study by combination, extension, and analogy, and in his liberty to create his own problems for investigation in which he pursues the behavior of his elements to the furthest depths his mind can penetrate. This liberty is highly prized by mathematicians. As Cantor put it, "Das Wesen der Mathematik liegt gerade in ihrer Freiheit" (The essence of mathematics lies just in its freedom). Nevertheless, this freedom has some peculiar consequences. When the mathematician finds that the problem which he has freely created is too hard for solution, he is still free to create an easier one—which he can solve and publish in a paper. With the freedom to set up all sorts of problems for solution it becomes more difficult to distinguish between trivial and important problems; and the doings of mathematicians may become controlled by temporary fashion or by the opinion of influential cliques. Nevertheless, these difficulties are also present to a lesser degree in the other sciences, and we often have to leave it to the future to decide what really was important.

The logicality of mathematics places a true limit on its creative freedom, since, above all else, the mathematician will demand that the results of his studies shall lead to mutually compatible conclusions. Indeed, at a fundamental level the disciplines of logic and mathematics have now tended to merge. On the one hand, this has come about from the invention of symbolic logic—the so-called algebras of logic—which lead logicians and mathe-

Address at the Graduate School Convocation of Brown University, June 14, 1947.

maticians to use the same kind of economical, shorthand language. On the other hand, and more important, it has come about from the contradictions to which mathematics is now being led as it pushes its studies further by what seem to be logical procedures. This means not only that mathematics provides a testing ground for what is logical, but also that the problems of logic have now become fundamental problems for mathematics itself.

This turn of affairs is so important that I shall try to give some idea of the way in which logical difficulties can arise. Mathematicians love to talk about sets of elements, for example, the set of three elements consisting of this pencil, this paper, and this desk—a perfectly simple idea. With their urge to create, they then like to talk about subsets of such a set, such as the subset containing the two members, pencil and paper or pencil and desk—still perfectly simple—or, even more, to create a new set consisting of all subsets containing two members—not quite so simple. In this way they are led to create a so-called set of all sets, which contains among its elements all possible subsets and all sets of such subsets. This leads to an infinite number of elements which is very pleasing to the mathematicians, since the properties of infinity are among the very things that they especially want to study. But now the trouble begins. On a piece of paper no larger than this we define some simple quantities applying to the elements of the set and define what seems to be a sensible subset. By a small computation we then calculate the value of one of our quantities for the subset and, to our amazement, suddenly obtain the value ½ for a quantity which by definition can only have the values 0 and 1. This is no trivial contradiction such as could be obtained by doing something foolish, like dividing by 0 or reasoning from an incorrect geometrical drawing. The mathematicians themselves do not agree as to what is wrong. Perhaps infinity will always make trouble; perhaps we have defined something that cannot exist; perhaps the logical principle of excluded middle is wrong. These are important questions. The presently shaken foundations of mathematical analysis depend upon the answers.

To the abstractions considered by mathematics, physics adds further elements, taken from the real world, which seem of a more palpable character. These include concepts as to physical space and time, the study of which has led to the Einstein theory of relativity; the concepts of mass, momentum, energy, and electricity, whose deeper treatment now finds expression in modern quantum mechanics; and the concept of fundamental structural particles such as electrons and protons, which constitute the subject matter of nuclear physics. The developments of relativity and of quantum mechanics, and progress in nuclear physics, have been the great happenings in physical science during the present century.

The theory of relativity has two branches: the special theory which treats the relativity of uniform motion in a straight line, and the general theory which treats the relativity of all kinds of motion and is thereby led to a theory of gravitation. The ideas of the special theory, obtained by an appreciation of the actual nature of spatial and temporal measurements, have now permeated the whole thinking of physics. We use them every day in the laboratory, for example, in treating the behavior of high-velocity particles or in calculating the energy of nuclear reactions such as those in the atomic bomb. We no longer find it strange that meter sticks should appear shortened and clocks slowed down, when in motion relative to our own measuring instruments. Indeed, we have now found mesotrons in the cosmic rays which, merely because of their high velocities, last 20 times longer than stationary mesotrons before changing over into electrons. It is now only the cranks, like circle squarers and angle trisectors, and Nazi "Aryan" physicists, who still remain worried by special relativity. The rest of us realize the inadequacy of old-fashioned space-time intuitions based on ancestral experience with slow velocities and have actually grown new space-time intuitions which make high-velocity phenomena seem reasonable and right.

The ideas of the general theory of relativity and its theory of gravitation have had much less impact on the ordinary thinking of physics. This is partly due to the fact that the Newtonian theory of gravitation is plenty good enough for the laboratory, and that the three crucial tests of general relativity have to do with small astronomical effects. In addition, the nonlinear equations of general relativity are extremely troublesome to handle, and this has led to a recent attempt at a linear theory of gravitation, for which I cannot myself see adequate motivation. As nearly as I can see the future, the relativity theory of gravitation provides a basis from which we shall go forward, not backward. Recent English opinions that Hubble's observations disprove the relativity treatment of the recession of the nebulae are not sound; the most that such observations could now do would be to disprove the adequacy of some particular model of the universe. In this connection, I have two pleasing bits of astronomical information to impart. Observations on nearby nebulae, made in recent years at Mount Wilson and at Mount Hamilton, now give strong additional evidence for the belief that the red shift in light from distant nebulae is actually due to their motion away from us, as assumed in the relativity treatment. The final figuring of the 200-inch mirror in Pasadena is now so nearly perfect that we can confidently expect its completion this summer. The mirror will then go up to join the telescope mounting, which waits for it on Mount Palomar, and we can look forward with excitement to the new knowledge of the structure of the universe which this greatest of all telescopes will bring.

We must now turn to quantum mechanics, which has

ven us the greatest advance in theoretical physics since ativity. As in the case of relativity, this advance has ulted from clear thinking with regard to the actual ture of the results of physical measurement; its consquences have now permeated the thinking of the boratory; and it has led to new and improved ideas conrning the nature of the physical world. The full delopment of quantum mechanics, however, can not yet regarded as complete, since so-called infinity difficuls persist when we attempt to push on.

Among the new and improved ideas provided by antum mechanics are some striking conclusions conrning the true relation between cause and effect. In reement with the Heisenberg uncertainty principle, we w see that a complete knowledge of the state of a physil system at any given instant is not sufficient to permit exact prediction of that system's future behavior. The st that we can do is to make statistical calculations ncerning the future behavior that can be expected on e average. As a consequence, we now have to regard e true connection between physical cause and effect as statistical one and give up the idea that the behavior the physical world is strictly determined.

This still seems very distressing to Einstein, who says, Der Herr Gott wurfelt nicht" (The Lord God does not row dice). Most of us, however, are quite content with e outcome. We do not see how any other outcome would possible in view of the uncontrolled disturbances inoduced by the very act of observation. We appreciate at past intuitions as to the exact connection of cause d effect were based on experience with those very tuations where the disturbing effects of observation are o small to be noticed. And we are happy that possibilies for statistical prediction still remain, since, without me possibility of prediction, science itself would surely e destroyed. I must caution you, however, that the inion of one good physicist that the uncertainty rinciple brings free will and moral responsibility back to the world can hardly be regarded as sensible. As far I know, moral responsibility has never left the world d, indeed, could hardly be helped by a principle which akes physical happenings, to the extent that they are ot determined, take place in accordance with the laws pure chance.

Now to nuclear physics, where we delightfully arrive an old-fashioned kind of science in which the experenters find out new things faster than the theoreticians n predict them, and sometimes in contradiction thereto. he important recent events in this field have been the perimental discovery of the new particles—neutron, ositron, and mesotron—now added to the previously nown electron and proton, and the experimental study the properties and behavior of the different kinds of uclei which are composed from such fundamental articles. It is these different kinds of nuclei which give s the different kinds of atoms and substances that exist in the world. It will be of interest to mention three examples of the interplay between experiment and theory in this field of work.

The existence of the positron—a positively charged electron—had not been theoretically predicted before its discovery in cosmic rays by Anderson, but an existing attempt by Dirac at a theory of the proton was then immediately seen to give at least a partially satisfactory explanation of the positron instead. The existence of a particle like the mesotron had been theoretically assumed beforehand by a Japanese named Yukawa, in order to explain the forces holding protons and neutrons together in nuclei. Actual mesotrons, which are like electrons but 200 times as heavy and with an average life of only 2.15 millionths of a second before they change over into electrons, were then discovered in cosmic rays by Neddermeyer and Anderson, but have so far not proved successful in explaining the forces that hold protons and neutrons together. The disintegration of uranium nuclei by fission, which led to the invention of the atomic bomb, had not been theoretically predicted before its discovery by Hahn and Strassmann. However, immediately on discovery, this phenomenon was seen to be reasonable on the basis of simple theoretical considerations of Bohr as to the nature of heavy nuclei.

I must complete these words on nuclear physics with a remark about a horrible little particle called the neutrino. No direct effect from neutrinos has ever been found; their existence has been assumed merely for the purpose of carrying away energy and momentum that would otherwise seem to be destroyed. This is very unsatisfactory. Perhaps it would be better to abandon the idea of the conservation of energy rather than to invent a new particle that one can never find.

I hope that the foregoing gives some right ideas as to what is happening in physics. There are other things which I should like to talk about, such as the important work of Prof. Lindsay, of this University, on the philosophical bases of physics, but these deep matters will have to be a subject for private conversation with him.

We now come to the science of chemistry, which adds, to the physical notion of the existence of matter in general, the more specific concept of many different kinds of chemical substance and of chemical reaction from one kind of substance to another. In this connection, however, I must now tell you of an important change that has taken place in our thinking. With the help of the new quantum mechanics, and of our new ideas as to the nature of electrons and nuclei, we now find it possible to give an adequate explanation of chemical substance and chemical reaction in terms of the concepts of physics. Thus, a minor revolution has taken place in the organization of science. We now no longer regard chemistry as a science separate from physics but rather as one of the group of physical sciences in which, for example, we also include kinematics, mechanics, and electrodynamics.

I call this revolution a minor one for several reasons. The explanation of chemistry in terms of physics is a revolution that was long impending and, indeed, expected and desired by many chemists, but one which could not be consummated until quantum mechanics had furnished the proper tools. The revolution has not eliminated the necessity of providing different kinds of atoms to explain chemical substances and reactions, but has merely transferred to physics the task of building such atoms out of electrons and nuclei. Finally, the revolution has had little impact on much significant chemical work, since the theoretical possibility of going back to quantum mechanics for explanation is often neither practical nor profitable. Thus, it would often be foolish to describe in quantum-mechanical language the results of the work in physical and inorganic chemistry which has been carried out at Brown University by Prof. Kraus and his colleagues, and which has been so important in peace and in war. Similarly, in the important applications of organic chemistry to biological problems, quantum-mechanical language is not usually appropriate.

Let us now turn to the field of biology. To a physicist who, like myself, still remains a human being, this would seem to be a wonderful science, with possible answers to all the important questions of life. It would be so easy if we could just say that "life" is the new abstraction that must now be added to those of physics and chemistry to get the science of biology, and that this science will then tell us all we want to know about life, death, freedom, and immortality. I think, however, that actually we have to say something much more nearly like the following.

We now add a new kind of abstraction, that of the so-called living organisms. These are material bodies which can maintain themselves, at least for a time and in a properly selected environment, in a substantially steady state through a continuous interchange of matter, energy, and entropy with their surroundings; which are irritable to external stimuli and can adjust to moderate changes in environment; which, under suitable conditions, can exhibit possibilities for growth, change in form, and reproduction in kind; which present themselves to our attention as a series of many different but not unrelated species; and which exhibit the influence of a long past history of evolutionary change as an essential determinant of present structure and behavior.

The difference between biological and physical-chemical work is frequently characterized by the intimate dependence of biological material on its environment and its essential dependence on the specific history of its past evolution. Indeed, the essence of a good physical-chemical experiment, when we are not concerned with cosmological problems, is usually to free the outcome from such dependence. Thus, a mixture of hydrogen and oxygen should explode whether we prepare the gases ourselves and store them in bottles or buy them already prepared and stored in tanks. But the behavior of plants and animals is always delicately dependent on sunlig and food and is essentially dependent on a particula series of evolutionary changes that have taken place i the recent past—in the last 100,000,000 years or ofte much less.

I wish that I were competent to tell you about th extraordinarily interesting things that are happening i biology. The last sweeping innovation in this field sti appears to be the genetic explanation of the factors co trolling heredity, given by Morgan and his colleague It is comforting to appreciate the extent to which ou own behaviors are determined by the genes, provided b our fathers and mothers, since we can't do anything abou it ourselves. Recent happenings in genetics include elaborate mathematical analyses of the rates at whic evolutionary changes can take place through gene muta tion; laboratory observations on the action of the enviro ment in selecting for survival different mutant forms o bacteria; further experiments on the artificial productio of mutations and on the possibility for the specific contr of such mutations; and studies of the chemical processe by which genes determine the behavior of the rest of a organism, which have been greatly furthered by Beadle' recent introduction of *Neurospora* as an especially con venient genetic material.

In the field of biochemistry great things are also hap pening. They include studies on the action of enzymes— hormones, vitamins, and others—in controlling biochemi cal reactions; advances in immunology, where the lock and-key-like behavior of antigen and antibody seem significant; further work on the structure of the proteins where the template-like pattern of complicated molecule plays such an important role; and studies of the tobacc virus and other similar viruses, where such a simpl physical-chemical structure is found that we have t regard these substances as lying at the boundary betwee inert and living matter. To the physicist, biology is th green pasture beyond the fence where it would be goo to roll in the long grass.

We must now pass on to psychology, which is the leas abstract of the sciences for which we shall have time Here it would be simple if we could just take "mind" a the further abstraction from reality that has to be adde to those of biology to arrive at psychology, but things no become so complicated that the psychologists themselve are not yet well agreed. For myself, I should at the pre ent moment like to say something about as follows. W now add the new abstraction of a special kind of behavio commonly called mental, which characterizes the activit of individual organisms as a whole, which frequentl appears purposive in character, and which includes th verbal behavior of ourselves and of others when giving a introspective account of our own sensations, feelings, an thoughts. Certainly a very poor statement, containin ill-defined and unanalyzed concepts, but at least omittin or covering up in its verbiage that bothersome wor

"mind." We are indebted to the work of the behaviorists, including the important contributions of Prof. Hunter, of this University, for a view of psychology which emphasizes observable behavior rather than hypothetical mind. This leads at once to the first of two comments on psychology.

As a consequence of the ease with which we often distinguish between what we call physical, and what we call mental, behavior, it seemed natural in the past—and indeed long ago in the past—to introduce the two separate abstractions of body and of mind. By doing so, however, we immediately threw ourselves open to that sea of troubles, the so-called body-mind problem. Having divided our man up into a separate mind and body, what should be the interaction between these two disparate entities, and how should we ever get the whole man back together again? Increasingly in the last years these theoretical difficulties have been augmented through observation and practice in the field of psychosomatic medicine—for example, recognition in military medicine of the psychogenic factors in the nevertheless real rheumatism of soldiers. In general, we often find, on the one hand, unconscious desire to escape into ill health producing the corresponding physical symptoms, and, on the other, the presence of bodily health fostering mental serenity and sanity. In such connections it seems probable that our scientific abstractions will in the future become more appropriate.

The second comment has to do with the revolution in psychology brought about by the psychoanalytic doctrine of Freud. As to this, much controversy has raged, and some academic psychologists are still disturbed, even when the language and explanations of psychoanalysis are already issuing from their lips. From a pragmatic point of view psychoanalysis certainly proves useful—in the treatment of neuroses, in the treatment of a restricted class of psychoses, and, above all, in our daily lives when we must try to understand the motives both of ourselves and of others. Indeed, in view of its present expense, perhaps we ought to say, "What this country needs most is a good five-cent psychoanalysis." The various methods of so-called "short therapy," recently introduced through the exigencies of military psychiatry, may be a step in that direction. From a theoretical point of view much remains to be done. The better incorporation of psychoanalytic doctrine into the main body of psychology must be pursued further; the already-fruitful study of the relations between psychoanalysis and cultural anthropology must be continued; and, above all, the present vigorous development of psychoanalytic theory must not be stopped, even by Freudian scholastics who regard themselves as the only true guardians of the pure faith.

Psychology must be the last of the various sciences to which we give detailed attention. We have now gained a reasonable idea of the kind of things happening in the different sciences and the methods by which we proceed from one science to another by including further features of the actual, concrete world around us. By continuing the procedure we could presumably go on to social psychology and the social sciences in general, although perhaps with considerable difficulty and uncertainty.

So far consideration has been given to the so-called pure sciences, each of which has the task of determining the principles that explain its own particular field of phenomena. We must now give a word to the so-called applied sciences, in which these principles are employed in other fields. For the layman, the term applied science usually implies application to practical or industrial ends, such as the navigation of ships or the manufacture of radios, but for the scientist, the term also includes, as of special interest, the application of the principles of one science to another.

Of all the applied sciences, applied mathematics is the most important, since its methods are needed and used in all the other sciences. This usefulness does not seem surprising, for, as we have seen, mathematics selects for its study those simple and general elements which will also often be present in the situations studied by other sciences. In addition, mathematics has invented such a clear and economical language for the logical treatment of complicated problems that the other sciences also find it useful as they themselves become more complicated. As an illustration, we, nowadays, even find psychologists writing books on that very difficult subject, the mathematical theory of statistics—and they do not do so badly at it either.

In view of the importance of applied mathematics, I wish to pay special tribute to Dean Richardson who, in addition to his own notable contributions to pure mathematics, has had the sagacity and ability to foster the establishment and activities of the Brown University Institute of Applied Mathematics. We may look on the present and future accomplishments of this Institute with satisfaction and confidence.

Just as mathematics, the most abstract of the sciences, can be applied to all the others, each of the various pure sciences can be applied to those that stand above it on the ladder of abstraction. Thus, the applications of physics and chemistry to biology are now proving extremely fruitful in the explanation of biological phenomena that we could not otherwise understand. Indeed, the study of biology with the help of physical-chemical methods is a rich vein which will not be worked out for many decades. This brings us to a consideration of the problem of the extent to which the phenomena of any science can be explained in terms of the more abstract sciences below it. Perhaps all of biology and psychology—life and mind themselves—might be explained in terms of physics and chemistry. This would be pleasing to some persons, including some pretty good scientists.

This important question, as to the extent to which a given science can be explained in terms of more abstract ones, is always present in my own thinking. I believe that the answer depends on the extent to which the science in question has really introduced genuinely new abstractions from reality, beyond those already incorporated in the preceding sciences below it. On this basis, I myself feel led to the following tentative conclusions: on the one hand it is my conviction that the phenomena of biology and psychology will never be found to contradict the principles of physics and chemistry. On the other hand, it is my belief that such principles will perhaps not prove sufficient for the full explanation of biology and will almost certainly not be sufficient for the explanation of psychology.

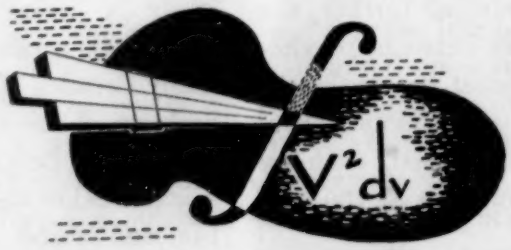
Finally, I wish to say something about the application of the sciences to so-called practical ends. In the first flush of enthusiasm for the industrial revolution that resulted from the practical applications of science, it was felt that the consequences of such application could only be for the good of man. As we have seen more of these consequences, however, and thought more deeply on such matters, we now realize that the practical results of science will be good or evil, in the ethical sense, depending on the nature of the application. This conclusion is dramatically illustrated in the scientific development of atomic energy which can be used either for peaceful or destructive purposes. The possibilities for evil are clear in the development of a weapon which could be used, in a surprise attack before any declaration of war, for the destruction of a score of cities and most of the inhabitants thereof.

The evils that can result from wicked application do not mean that science itself is evil. Each pure science merely gives an objective account of the facts which it finds in its own field of study. These facts are ethically neutral; it is only their application that can lead to evil rather than good results. Moreover, from a broader and deeper point of view, the pursuit of these ethically neutral facts must itself be regarded as a good. It is a spiritual good, since knowledge of the true nature of the world in which he lives should increase the intellectual dignity of man. It is a practical good, since it is only through knowledge of the actual facts that men of good will can plan for their application to good rather than evil ends. Keeping certain facts secret, as in the field of atomic energy, can be temporarily important and serve a useful purpose, but can make no fundamental contribution to the prevention of evil.

In the control of evil, psychology and the social sciences have a special role to play. This resides in the provision of information and advice concerning the human and social consequences of different courses of action—for example in establishing international control of atomic energy. It does not reside in any ethical quality pertaining to these sciences themselves. The objective findings of psychology are as ethically neutral as those of any other science and can be applied not only to good but also to evil ends, as in determining the most effective form for sinful propaganda such as that of the Nazis. Even when the anthropologist studies the moral practices and systems of different tribes and nations, his findings remain objective and ethically neutral and contain, as science, no recommendation of one set of moral values over another. Science is concerned with judgments of existence, not judgments of value.

The judgments of men and of nations of men as to what is good depend partly on the static factors of childhood training and of prevailing custom, but partly also on the dynamic consequences of the new spiritual insights which determine the teachings of ethical leaders and which each of us may sometimes experience in the closet of his conscience. As the judgment is being reached science can advise as to the nature of the facts. When the judgment is being advocated, science can point out its consequences. When the judgment is being implemented science can supply tools for the accomplishment. But in its final essence, ethical judgment is a creative activity of man.

It is my faith that the ethical insight and scientific intelligence of man are such that the control of evil is possible. I am sure that humanity will continue to encounter great troubles, but I do not think that civilization will destroy itself. To surmount our troubles, we shall need courage, patience, clarity of thought, and sincerity in the advocacy of fair and reasonable courses of action. For these virtues we may pray, each in his own fashion.



# NEWS *and Notes*

**The National Science Foundation bill,** after having been passed by both the House and Senate, was vetoed by President Truman on August 6. At the same time the President urged that Congress, when it reconvenes in January, reconsider and pass an acceptable bill. The veto message stated that the bill implied "a distinct lack of faith in the democratic process" and, in effect, would "vest the determination of vital national plicies, the expenditure of large public funds, and the administration of important governmental functions in a group of individuals who would be essentially private citizens." It went on to say that "full governmental authority and responsibility would be placed in 24 part-time officers whom the President could not effectively hold responsible for proper administration. Neither could the director of the Foundation be held responsible by the President, for he would be an appointee of the Foundation and would be insulated from the President by two layers of part-time boards."

Watson Davis, director of Science Service, in a release dated August 7, has aptly commented: "Scientists in all fields are disappointed that the bill did not become law. Some of them point out that control of research funds available for grants are left, by default, largely in the hands of the Army, Navy, and Air Force . . . they want to see research predominantly in civilian hands, and the military research bureaus have agreed with them. Scholarships for young research scientists were authorized in the bill as an aid to filling the depleted ranks of scientific investigators. This is considered one of the most important functions of the foundation, now delayed."

**Network television operations were expanded on June 27,** when station WNBW (NBC) went on the air. Located in Washington, atop the Wardman Park Hotel, the new station is linked by coaxial cable with station WNBT in New York. Using a new postwar television transmitter, type TT-5A, developed by RCA, the station will operate on Channel 4. The picture signal of the transmitter is built up to 20.7 kw. when radiated from the turnstile antenna on the 350-foot tower on the hotel. Network operations on a national scale are to be considerably expanded during 1948. Present coaxial cable facilities now extending from New York to Philadelphia, Washington, Richmond, and Charlotte, North Carolina, will be connected with a cable already installed between Jacksonville, Florida, Atlanta, Jackson, Mississippi, Shreveport, Louisiana, and Dallas. Installation of the cable from Charlotte through Augusta to Atlanta and from Dallas to Los Angeles will complete the first coast-to-coast network.

## About People

**Donald A. Keys,** chairman, Department of Operative Dentistry, University of Nebraska, will give a series of lectures beginning August 23 to members of national dental associations in Norway, Sweden, and Denmark, to help bring dentists in these countries up to date on recent American developments in dentistry. Dr. Keys will return late in September.

**Charles E. Kellogg,** chief, Division of Soil Survey, U. S. Department of Agriculture, returned July 24 from a three-month visit in Europe and Africa. He attended the Mediterranean Conference of Pedology in southern France and Algeria, took part in a small conference held in Paris to plan for reorganization of the International Society of Soil Science, and visited the Rothamsted Experimental Station and the University College of North Wales. As the guest of INÉAC (Institut National pour l'Étude Agronomique du Congo Belge) he traveled for 5 weeks in the Belgian Congo, visiting experimental stations and studying soils and agriculture in the field.

**Robert J. Coffey,** former fellow of the Mayo Foundation, has been appointed professor of surgery, Georgetown University, Washington, D. C., effective July 1.

**R. H. Rigdon,** formerly professor of pathology, University of Arkansas Medical School, has been appointed professor of experimental pathology and director, Laboratory of Experimental Pathology, University of Texas Medical Branch, Galveston.

**Winthrop Perrin Haynes,** geologist, Standard Oil Company of New Jersey, has been appointed visiting lecturer in geology, Harvard University, for the academic year 1947–48. Dr. Haynes will give courses in Petroleum Geology.

**Ralph T. Holman,** now on leave from the Department of Physiological Chemistry, University of Minnesota, will join the Department of Biochemistry and Nutrition, Agricultural and Mechanical College of Texas, about February 1, 1948. Dr. Holman is now doing postdoctorate work at the Nobel Institute of Medicine, Stockholm, and before returning to this country will spend several months with Prof. Tiselius at Uppsala.

**Arthur W. Grace,** professor of clinical dermatology and syphilology, Long Island College of Medicine, left on July 27 for a 7-week lecture tour of South America during which he will visit 6 countries. His trip is sponsored by the E. R. Squibb & Sons Inter-American Corporation and the Squibb Institute for Medical Research as part of a program to stimulate the exchange of advances in research, practice, and medical education between the two continents.

**Raymond H. Fletcher,** former director of instruction, Highland Park Schools, has joined the Texas regional office staff of Rohrer, Hibler and Replogle.

**Fritz Schlenk,** professor of biochemistry, University of Texas Medical School, has been appointed professor, Department of Bacteriology, Iowa State College, and **Paul Arne Hansen,** recently associate bacteriologist in charge of a field station for the U. S. Department of Inte-

rior at Hampton, Virginia, has been appointed associate professor.

**Robert B. Dean,** formerly at the University of Hawaii, **Hans Heymann,** Harvard University, **Francis J. Reithel,** California Institute of Technology, and **Donald F. Swinehart,** Los Alamos Laboratory, have recently been appointed assistant professors in the Department of Chemistry, University of Oregon, Eugene.

**William B. Deichmann,** head of a Division of Toxicology, Kettering Laboratory of Applied Physiology, University of Cincinnati, since 1939, has been named associate professor of physiology and pharmacology and head, Division of Pharmacology, Albany Medical College, Albany, New York.

**Lawrence M. Richards,** formerly on the research staff of the DuPont Experiment Station, Wilmington, Delaware, is now associated with the Stanford Research Institute as a research chemist.

**John B. Patton,** geologist, Magnolia Petroleum Company, Mt. Vernon, Illinois, has been appointed research associate in economic geology, Department of Geology, Indiana University.

**L. C. Graton,** professor of mining geology, and **Francis Birch,** professor of geophysics, both of Harvard University, have been sent to Iceland by the Committee on Experimental Geology and Geophysics at Harvard to observe geysers and other thermal phenomena.

## Industrial Laboratories

**The Calco Chemical Division, American Cyanamid Company,** Bound Brook, New Jersey, has recently announced that **Robert P. Parker,** former head, Pharmaceutical Section, Research Department, has been appointed assistant research director; **Erwin Kuh,** Pharmaceutical Research Department, research associate; and **James Smith,** formerly of the University of Virginia, and **J. J. Denton,** Organic Section, Research Department, assistant chief chemists.

**At the General Electric Research Laboratory** David Harker and J. S. Kasper have developed a method for determining the way in which atoms are arranged in a complicated crystal. The method, which involves mathematical analysis of the patterns obtained when X-ray beams are shot through the crystals, may furnish important information about the structure of proteins. The atoms of a crystal, which have some regular arrangement, diffract the X-rays, and the pattern is recorded on a photographic plate. Although it has been possible to measure the intensities of the rays extending from the crystal and making up the diffraction pattern, it has not been possible to determine their phases. With the new method the phases may be determined from the intensities of the rays, the mathematical analysis then providing a picture of the crystal's structure.

**Merck & Co., Inc.,** has named Randolph T. Major vice-president and scientific director; John H. Gage, treasurer; and Per K. Frolich, director of research and development, succeeding Dr. Major.

**H. A. Murray,** chief chemist and assistant plant manager, Best Foods, Inc., Buffalo, New York, since 1934, has been appointed manager of the Buffalo plant, succeeding **V. B. McLean,** who has retired. **Edwin L. Sexton** has been appointed chief chemist succeeding Dr. Murray.

**William Reiner-Deutsch,** microbiologist, Industrial Testing Laboratories, New York City, has been appointed director of research.

**Willis F. Harrington,** vice-president and member of the Executive Committee, E. I. du Pont de Nemours & Company, resigned August 1. Mr. Harrington, who will continue to serve as a member of the Board, is succeeded by **J. Warren Kinsman,** general manager, Fabrics and Finishing Department.

## Colleges and Universities

**The Department of Horticulture, Michigan State College,** has recently received an appropriation of $150,000 from the State Legislature for facilities and equipment for research.

**Case Institute of Technology** has announced the appointment of **T. Keith Glennan,** an executive of Ansco Division, General Aniline & Film Corporation, Binghamton, New York, and during the war, director, U. S. Navy Underwater Sound Laboratory, as its new president, succeeding **William E. Wickenden,** who will retire September 1.

**Kansas State College of Agriculture and Applied Science** is the recipient of a recent donation of $16,500 from the milling industry, to be used for equipping a pilot plant bakery to be operated in connection with the Department of Milling Industry. The new facilities will be used for research, wheat quality evaluation, and student training programs.

## Meetings

**The Mathematical Association of America** will hold its 29th summer meeting at Yale University, New Haven, Connecticut, September 1–2, in connection with the summer meeting and colloquium of the American Mathematical Society and the meeting of the Institute of Mathematical Statistics. The first session, to be held at 2:30 P.M. September 1, will include "Atomic Energy," R. C. Bacher, U. S. Atomic Energy Commission, and a symposium on "Mathematical Problems at the College Level." Participants will include: George Polya, Leland Stanford University, chairman; H. F. MacNeish, Brooklyn College, and J. L. Synge, Carnegie Institute of Technology, co-chairmen; and H. S. M. Coxeter, A. M. Gleason, P. G. Helsel, Tibor Rado, L. M. Kelly, and E. P. Starke, contributors. The second session, at 9:00 A.M. September 2, includes: "Mathematics for the Liberal Arts Student," Carl Allendoerfer, Haverford College; "The Mathematics Program in the College of the University of Chicago," E. P. Northrop, University of Chicago; and a symposium on "Computing Machines" at 10:00 A.M., in which H. H. Aiken, Harvard University, and John Von Neumann, Institute for Advanced Study, will participate.

**The 77th meeting of the American Astronomical Society** will be held September 3–6 at Dearborn Observatory, Northwestern University, Evanston, Illinois, at the invitation of Oliver J. Lee, director of the Observatory. A special session will be held September 6 at Yerkes Observatory, Williams Bay, Wisconsin, to celebrate the 50th anniversary of the founding of the Society and Yerkes Observatory. Papers by members will be presented during the morning and afternoon sessions, September 4, and

the morning session, September 5. The business meeting is also scheduled for September 4, and the teachers' conference for the afternoon of September 5.

**The Chicago Section, American Chemical Society,** will hold its third All-Day Technical Conference on December 26 at Hotel Sherman, Chicago, in conjunction with the 114th AAAS meeting. A joint three-day chemistry program will be featured by three symposia organized by the Chemistry Section, AAAS, and by a series of divisional meetings conducted by the Chicago Section, ACS. Although this conference is being sponsored by the local Section, contributions from other areas will be welcome. Titles must be submitted by September 20 to the following divisional chairmen: (I) Biological and Pharmaceutical—L. W. Clemence, Abbott Laboratories, North Chicago, Illinois; (II) Chemical Education—T. A. Ashford, Department of Chemistry, University of Chicago; (III) Agricultural and Food—G. A. Crapple, Wilson & Company, 4100 S. Ashland Avenue, Chicago 9; (IV) Industrial and Engineering—Kenneth Anderson, Northwestern Technological Institute, Evanston; (V) Inorganic and Analytical—George Gibson, Illinois Institute of Technology, 3300 Federal Street, Chicago 16; (VI) Organic—M. M. Gladstone, Emulsol Corporation, 59 E. Madison Street, Chicago 2; (VII) Petroleum—S. B. Becker, Standard Oil Company (Indiana); 910 S. Michigan Avenue, Chicago 5; (VIII) Physical—H. E. Ries, Jr., Research and Development Department, Sinclair Refining Company, East Chicago, Indiana; (IX) Radiochemistry—W. F. Libby, Institute for Nuclear Studies, University of Chicago. Further information may be obtained from Miss Mary Alexander, Conference Committee Secretary, Universal Oil Products Company, 310 S. Michigan Avenue, Chicago 4.

**The Oregon Geography Council** will hold its fall conference October 4, at Memorial Union Building, Oregon State College, Corvallis. The evening dinner program will be held in the Benton Hotel. The morning session on the general topic, "Regional Planning: A Practical Application of Geography," will offer lectures by E. L. Ballard, Oregon State College, "Planning for Agriculture in Oregon"; F. Arpke, Bonneville Power Administration, "Business and Industrial Planning in Oregon"; and Chester Sterrett, Portland Chamber of Commerce, "Urban Planning in Oregon." During the afternoon program on the topic, "The Climatic Factor in Geography," Phil Church, University of Washington, will speak on "Climatic Regions as an Approach to World Geography," after which there will be sectional meetings to discuss instructional problems in modern geography. At the evening meeting, new officers will be installed, and Howard H. Martin, University of Washington, will speak on "Geography in World Affairs." Further information may be secured from J. Granville Jensen, Department of Geography, Oregon State College, Corvallis.

**The Tri-State Field Conference,** consisting of staff members and graduate students of universities, colleges, and State Geological Surveys in Wisconsin, Iowa, and Illinois, is to be held this year in Wisconsin, probably early in October. W. H. Twenhofel will lead the group through the Silurian of eastern Wisconsin. L. M. Cline, Department of Geology, University of Wisconsin, is chairman of the Arrangements Committee.

**The Electrochemical Society, Inc.,** is planning a Boston Congress on October 15–18. Headquarters for the Congress will be the Copley-Plaza Hotel. Scientific sessions will be held on such topics as The Per Salts, Electrochemical Methods of Laboratory Control, Electrodeposition—1947, New Primary Cells, and Electroorganic Syntheses. Charles G. Harford is chairman of the local committee making arrangements for the meetings.

## Elections

**The Pacific Section, Botanical Society of America,** at a recent meeting, elected the following officers: Lyman Benson, Pomona College, president; Ralph Emerson, University of California, Berkeley, secretary-treasurer; and Walter S. Phillips, University of Arizona, representative on the Council of the Pacific Division, AAAS.

**The Institute of Navigation,** at its annual meeting on June 23–24 in Washington, D. C., elected the following national officers for the academic year 1947–48: Commodore G. G. McLintock, USMS, special assistant to the Commandant, U. S. Maritime Service, Washington, D. C., president; Capt. P. V. H. Weems, USN (retired), Annapolis, Maryland, vice-president; Paul Rosenberg, president of Paul Rosenberg Associates, New York City, technical adviser; and Samuel Herrick, professor of astronomy, University of California at Los Angeles, executive secretary.

## NRC News

**Lewis H. Weed,** chairman of the Division of Medical Sciences, recently returned from England, where he received the honorary degree of Doctor of Laws from Birmingham University. The degree was conferred upon Dr. Weed on July 4 during ceremonies at the University at which the chancellor, Anthony Eden, officiated. The citation accompanying the degree referred to Dr. Weed as "the greatest living authority on the nature and functions of cerebrospinal fluid" and paid tribute to his work in embryology as well as to his outstanding work with the military services during the war years. Dr. Weed recently resigned as professor of anatomy at Johns Hopkins Medical School in order to devote full time to his duties as chairman of the Division of Medical Sciences.

## Recent Deaths

**John Samuel Houser,** 66, chief, Department of Entomology, Ohio Agricultural Experiment Station since 1926, died June 25 at his home in Wooster, Ohio.

**Arthur LaMotte,** 76, formerly manager, Technical Service Section, Explosives Department, E. I. du Pont de Nemours and Company, died July 17 in Oakland, California.

**Leo Everett Hudiburg,** 49, professor of physics, Kansas State College, and former assistant dean, School of Arts and Sciences, died July 23 at his home in Manhattan, Kansas.

**Treat Baldwin Johnson,** 72, Sterling professor of organic chemistry, Yale University, prior to his retirement in 1943, died July 28 at his home in Bethany, Connecticut.

**Charles Franklin Curtiss,** 83, dean emeritus of agriculture, Iowa State College, died July 30 in Ames, Iowa.

**Hubert Lyman Clark,** 77, associate professor emeritus of zoology, Harvard University, died July 31 in Cambridge, after a month's illness.

**Robert B. Thomson,** 76, professor emeritus, and head, Department of Botany, University of Toronto, until his retirement in 1941, died July 31 in Agincourt, Ontario, following an illness contracted last year while representing Canada at the All-India Scientific Congress.

**Orrin C. Blair,** 69, chairman, Lynn Cancer Clinic, died August 3 at the Lynn Hospital, Massachusetts.

**Henry Harold Higbie,** 64, professor of electrical engineering, University of Michigan, died August 3 in Ann Arbor, after a brief illness.

**D. E. Lea,** 37, British radiobiologist, died recently in England as the result of an accident. Dr. Lea was the author of *Actions of radiations on living cells* (reviewed in the April 25 issue of *Science*) and, in collaboration with D. G. Catcheside, had formulated a detailed theory of induced lethals in *Drosophila.*

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**The editorial offices** of *Cancer Research* have been moved from New Haven, Connecticut, to the Medical School, University of Pennsylvania, Philadelphia 4. Balduin Lucké is succeeding S. Bayne-Jones as editor, and Morton McCutcheon will serve as associate editor. Edward W. Shrigley, of New Haven, continues as editor of the Abstracts Section.

**Rich collections of fossils,** made in the course of his field work in the Cerro de Pasco region of central Peru, under a grant from the American Philosophical Society, were sent in 1941 by William F. Jenks, University of Rochester, to Otto Haas, American Museum of Natural History, for identification. Since then, collections of Peruvian fossil invertebrates made from 1943 to 1946 by Norman D. Newell, of the Museum and Columbia University, Bernhard Kummel, Bureau of Economic Geology, Austin, Texas, and Dr. Jenks have been added to the initial material. Most of these collections are of Mesozoic age.

Although it was originally planned that Dr. Haas should take care of the study of all the collections from the Cerro de Pasco region, because of the addition of new materials and the unexpected multiplication of the total of fossils by means of chemical preparation, the work is being divided among several specialists. A report on charophytes from various regions and horizons, prepared by Raymond E. Peck and Mr. Reker, both of the University of Missouri, is intended for publication in the Museum's *Novitates;* John W. Wells, Ohio State University, will study the Anthozoa and Porifera; Dr. Newell, the pelecypods; Dr. Kummel, Triassic cephalopods; and Dr. Haas, the post-Triassic cephalopods and the gastropods. Some important groups, especially the brachiopods, second only to the mollusks in number of specimens, are still waiting for specialists to undertake their study. All of this work is being done in close cooperation with the Geological Institute of Peru.

According to present plans, a series of paleontological monographs on the Mesozoic of Peru will eventually be published, probably in the Bulletins of the American Museum of Natural History. As yet, only two preliminary papers have been published, one by Vokes and Haas (*J. Paleontol.*, 1944, **18,** 293–294) and one by Haas (*Bull. geol. Soc. Amer.*, 1946, **57,** 1198–1199). Aside from Peck's and Reker's work, mentioned above, only the post-Triassic ammonites have been identified by Dr. Haas, and a preliminary age determination of Liassic corals has been made by Dr. Wells. Work on Triassic gastropods and pelecypods by Drs. Haas and Newell, respectively, has been in progress for some time. A Triassic age (upper Middle to Upper) is assigned to most of the fossils from the limestones between Cerro de Pasco, Huachón, and Tilarnioc (central Peru).

**Excerpta Medica, Inc.,** of Amsterdam, has recently undertaken a project involving the publication of 15 journals containing abstracts of world literature in the fields of clinical and theoretical medicine. All abstracts will be published in English and will be prepared by about 3,000 specialists all over the world under the supervision of some 400 editors. It is intended that the journals will both replace and extend such publications as the *Zentralblätter* and *Berichte.* Each sectional journal will be issued monthly. The sections include: (I) Anatomy, Anthropology, Embryology, Histology; (II) Physiology, Biochemistry, Pharmacology; (III) Endocrinology; (IV) Public Health, Social and Industrial Medicine; (V) General Pathology, Pathological Anatomy, Bacteriology; (VI) Internal Medicine; (VII) Pediatrics; (VIII) Neurology and Psychiatry; (IX) Surgery; (X) Obstetrics and Gynecology; (XI) Oto-, Rhino-, Laryngology; (XII) Ophthalmology; (XIII) Dermatology and Venereology; (XIV) Radiology; and (XV) Tuberculosis. General medical direction is in the hands of a Chief Editorial Board consisting of M. W. Woerdeman, A. P. H. A. de Kleijn, and W. P. C. Zeeman. The Williams & Wilkins Company, Baltimore 2, Maryland, is the sole agent for the United States, Canada, and Central America. A free booklet describing the series is available on request.

**Applications of atomic power** and its by-products in industry, medicine, and other peaceful fields will be the subject matter of a new monthly, *Nucleonics,* to be published by McGraw-Hill, beginning in September. Each issue will contain 80 or more editorial pages and no advertising. The subscription price is $15.00 per year.

**A national mental health program,** authorized by Congress in 1946 and implemented on July 8 by an appropriation of $7,500,000, will encompass (1) increased research in problems of mental health, (2) training of urgently needed personnel, and (3) increased support and stimulation to states in the development of adequate programs. In achieving the first of these objectives approximately $400,000 will be spent during the fiscal year 1948 in the form of grants-in-aid and research fellowships. Over $1,000,000 will be spent for grants to nonprofit institutions for developing and improving facilities for training personnel as well as for providing training stipends for 70 graduate students in psychiatry, 41 in clinical psychology, 40 in social work, and 58 in psychiatric nursing. A sum of $3,000,000 is appropriated to states for their local programs, which are to include one outpatient clinic for each 100,000 of the population, services to rural areas through traveling clinics, and demonstration clinics to be operated by the Public Health Service. The remainder of the funds will be used for field studies in mental hygiene and operation of Public Health Service hospitals for drug addicts and the mentally ill at Lexington, Kentucky, and Fort Worth, Texas. An additional appropriation of $850,000 is to provide for purchasing a site and drawing plans for

National Institute of Mental Health, be located in the vicinity of the District Columbia.

**The National Registry of Rare hemicals,** 35 West 33rd Street, Chigo 16, Illinois, lists the following wanted hemicals: 2-isoimidazole; 2,1,3-triaole; 4,1,2-triazole; furazan; 1,2,4-adiazole; 1,3,4-oxadiazole; isotetrazole; yridazine; pyrazine; quebrachitol; d-uercitol; cellopentaose; α-benzylpyridine; ydroxytyramine; epinine; 2,2-difluororopane; glucose 6-phosphate; 2-phosphoglyceric acid; 3-phosphoglyceric acid; nd hygrine.

**A comprehensive list of powder etallurgy patents** to date, including brief abstract for each invention, has een compiled by Raymond E. Jager nd Rolla E. Pollard, of the National Bureau of Standards, and is now available s NBS Publication M184 (*United States patents on powder metallurgy*) from he Superintendent of Documents, Washington 25, D. C., at $.30 per copy.

## Make Plans for—

**American Institute of Electrical** Engineers, Pacific General Meeting, August 26–29, San Diego, California.

**Mathematical Association of Amer-** ica, September 1–2, Yale University, New Haven, Connecticut.

**Fourth International Cancer Research Congress,** September 2–7, St. Louis, Missouri.

**American Astronomical Society,** 7th Meeting, September 3–6, Dearborn Observatory, Evanston, Illinois.

**First International Biometric Con-** ference, September 5–6, Marine Biological Laboratory, Woods Hole, Massachusetts.

**American Psychological Associa-** tion, September 9–13, Detroit, Michigan.

**American Roentgen Ray Society,** September 14–19, Atlantic City, New Jersey.

**American Chemical Society,** 112th National Meeting, September 15–19, New York City.

**American Association for the Advancement of Science,** 114th Meeting, December 26–31, Chicago, Illinois.

# COMMENTS *by Readers*

**The scientific world has no direct concern with the political side** of the conference between the Indonesian and Netherlands Governments deciding on their future relations. These negotiations, however, also involve the status of the scientific institutions on Java and Sumatra, which are of much more than local significance. This is to be regretted, since it is generally admitted that the direction of scientific work and its results have no national or political boundaries. This was typically shown in Java, where men from all nationalities have contributed to scientific biological knowledge of the tropics. Swiss (Hasskarl, Zollinger, Bernard, Vischer, Schweizer), German (Junghuhn, Rumphius), Danish (Jensen, Gandrup), Swedish (Booberg, Tengwall), American (Rands, Yampolski), Chinese (Tan Sin Hok, Tung), Indonesian, and Dutch scientists all contributed while being employed at government and private research institutes and experiment stations. Appointment to such positions was dictated not by political considerations but by qualification for the job. This made the agricultural experiment stations in the Netherlands East Indies among the best in the world.

Recently, alarming news has come from Java concerning these scientific institutions. Plans had been formulated to have all scientific services placed on a commonwealth basis. The Indonesians, however, have claimed complete control over them. This has been ceded to them by a preliminary Netherlands Government decree. Indonesians have been appointed as directors of the institutions, irrespective of their qualifications. Thus, a veterinarian has been named director of the famous Botanic Gardens in Buitenzorg.

This is not scientific direction but political control, which nowhere in the world has produced scientifically significant results. Is it not time for us scientists to act and prevent renewal of methods which were so disastrous in Germany? It has been suggested that the scientific institutions in the Netherlands East Indies be brought under the supervision and control of UNESCO, which would insure continuation of the high standards maintained in the decades before the Japanese invasion. An expression of opinion in this matter, directed toward our representatives on UNESCO, might give results. (F. W. WENT, *California Institute of Technology, Pasadena.*)

**In the spring of 1946** I observed that many wild plants of *Cornus florida* in the vicinity of Ann Arbor, Michigan, which I remembered as having borne pure white blossoms formerly, now produced pink flowers. The pink tint usually was uniform over any one plant, but it ranged from the slightest blush to a deep pink from plant to plant. None was seen which was quite as deeply colored as the red variety of *Cornus florida*, but some were near it.

In the present season all these plants again formed white flowers, making it apparent that the weather of the spring of 1946, one of the driest on record for the region, was responsible for the change of color. Although I have no record of it, the amount of sunshine must have been much greater than usual. The combination of much light and little water may have caused a great increase in anthocyanin formation paralleling the familiar *firing* of the lower leaves of corn in hot, dry weather. (CARL D. LA RUE, *Department of Botany, University of Michigan.*)

**Folliculinids are complex ciliated protozoans,** very similar to the better-known stentors. The stentors are found chiefly in fresh water; the folliculinids, mainly in marine and brackish water, although some have been recorded from fresh water in England, France, Switzerland, Canada, and Uruguay. Since they occur in so many remote points in all oceans, it is easy to assume that they will yet be found along the coasts of all lands.

That they occur in India was stated in 1916, but this publication was so deeply

buried in accounts of other animals that it has only recently been exhumed by H. Shrinivasa Rao, Deputy Fisheries Adviser to the Government of India, who communicated the facts to me.

Folliculinids fasten their dwellings to all sorts of inanimate and animate objects. Some seem to have uncanny ability to search out concealed places and may establish their dwellings within those abandoned by other small animals. Some locate on the outside of hydroids, and it is in association with the latter that they have been found in India.

Many small jellyfish that swim free in the ocean separated themselves from hydroids, like plants branching, and firmly fixed to objects of the ocean floor. Among these the genera called *Tima*, *Eirene*, and *Phortis* are much alike, and even specialists have not agreed as to which name to use. MacCrady, the pioneer student of jellyfish in America, described a species of *Phortis* from Charleston, South Carolina, and W. K. Brooks, in his studies of jellyfish of Beaufort, North Carolina, was able, in 1883, to rear the hydroid phase from this same rare jellyfish.

Another species of *Phortis* shines with exceptionally strong blue-green phosphorescence. In 1905 Browne took from the sea off Ceylon a jellyfish he named *Eirene ceylonensis;* however, Mayer, in his *Jellyfish of the world*, decided that this was really a *Phortis*—a conclusion also reached by N. Annandale when in 1915, as superintendent of the Indian Museum, he reared from this jellyfish the little hydroid he had discovered in 1906 and identified as *Campanulina*. The same sort of jellyfish taken from the sea off Ceylon by Browne suddenly appeared in great numbers in July 1915, more than 1,000 miles away, in a brackish canal near Calcutta, in the delta of the Ganges. The canal water had a salinity of but 1.0085, reduced to 15°C. In this canal, "far removed from the sea though connected at one point with the tidal waters of the Hooghly," the jellyfish were no longer found in September, when the monsoon rains probably further diluted the brackish water. From these little jelly-fish less than an inch in diameter were reared the *Campanulina* hydroids, scarcely visible to the naked eye. In this study the work of Annandale was continued by R. E. Lloyd, professor of biology at the Medical College, Bengal, and their combined results were published under the title "Hydrozoon *Campanulina ceylonensis* (Browne)" (*Rec. Ind. Museum, Calcutta*, 1916, **12**, 49–57). We quote from Lloyd's detailed account the following sentence—sole evidence of the occurrence of folliculinids in India: "The hydroid first found at Port Canning was living in association with the protozoan *Folliculina* and this organism also occurred among the colonies taken from the canal."

Dr. Rao's search in the collections of the Indian Museum revealed nothing in the way of slides or material bearing upon these folliculinids. Apparently Prof. Lloyd did not identify the species of folliculinid he observed, but as to Lloyd's identification of the group Dr. Rao writes that he has "no reason to doubt his identification of the infusorians he found on the hydroids of Port Canning."

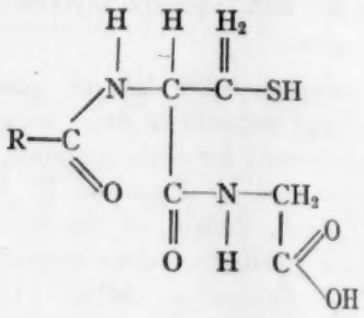
It is possible that other casual references to the occurrence of folliculinids in some corner of the world may remain hidden in the vast literature. Should anyone discover such hidden records, I would greatly appreciate being guided to them. (E. A. ANDREWS, *The Johns Hopkins University, Baltimore, Maryland.*)

**The differentiation of the pathogenic species of *Sporotrichum*** has always presented difficulties. It has been known since 1915 that carbohydrate fermentations, pigment formation, and production of chlamydospores are variable factors and cannot be used for the identification of species. In fact, the tendency among mycologists today is to regard the *Sporotrichum* pathogenic to man as one species.

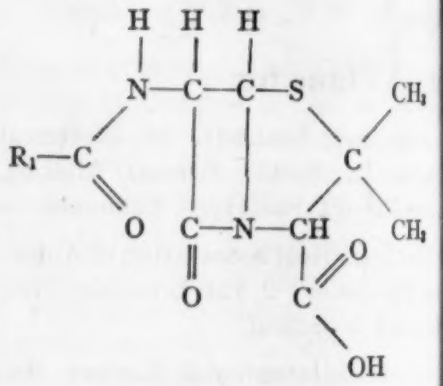
Sixteen strains of *Sporotrichum* representing examples of *S. schenckii*, *S. beurmanni*, *S. asteroides*, and *Rhinocladium equinum*, originating in America, Europe, and South Africa, were studied. Extensive agglutination and absorption experiments showed that these *Sporotricha* all have a common antigenic factor.

Details of this work are being published elsewhere. (H. I. LURIE, *South African Institute for Medical Research, Johannesburg.*)

**With reference to the interesting discussion** between C. S. Leonard (*Science*, November 29, 1946, pp.501–502) and C. J. Cavallito (*Science*, February 28, pp. 235–236) about the mode of action of penicillin, I should like to call attention to an interesting circumstance which I did not find mentioned in the literature available to me, *i.e.* the remarkable structural resemblance between penicillin and glutathione. In fact, the thiazolidine ring of penicillin may be imagined as resulting from a double ring closure between the β-methyl group of cysteine and the amino group of glycine on one side and between the SH group of cysteine and the α-methyl group of glycine linked together by a (dimethyl)-methyl radical on the other side (Fig. 1).




Glutathione




Penicillin

FIG. 1

From this point of view the terminal groups of penicillin would be characterized by a double ring formed between certain members of the open chains of the cysteyl-glycine radical through the intervention of a dimethyl methane, which would blockade irreversibly the SH group of cysteine. The glutamyl radical of glutathione is replaced with different other acyl radicals in the different classes of penicillin (pentanoyl, heptanoyl, valeryl, phenylacetyl, etc.).

It would be too far-reaching to draw without experimental basis any conclusion from this circumstance, but one may think of the possibility of penicillin competing with glutathione for enzymatic or other mechanisms important for microbial reproduction. (E. FISCHER, *Experimental Laboratory, S. A. Organa, Santiago, Chile.*)

# TECHNICAL PAPERS

## Inhibitory Effects of Ethyl Carbamate on Prostatic Cancer[1]

CHARLES HUGGINS, SUNG TING YÜ, and RALPH JONES, JR.

*Department of Surgery, University of Chicago*

The antiandrogenic treatment (*7*) of human prostatic cancer is not completely satisfactory, since remission of the disease was less than 5 years in duration in 80 per cent of the cases (*6*) so treated. We have investigated many possible chemotherapeutic agents in patients in whom relapse has occurred after endocrine control, but have encountered only one effective agent in ameliorating the disease when it has become androgen independent and wide spread—ethyl carbamate. Prostatic cancer may be studied simply by enzymatic methods, since the phosphatases of serum constitute sensitive and objective indices of neoplastic activity.

Warburg (*12*) showed that phenyl urethane in small amount caused an arrest of mitosis and cell division in fertilized eggs of the sea urchin with only small change in oxidation in the

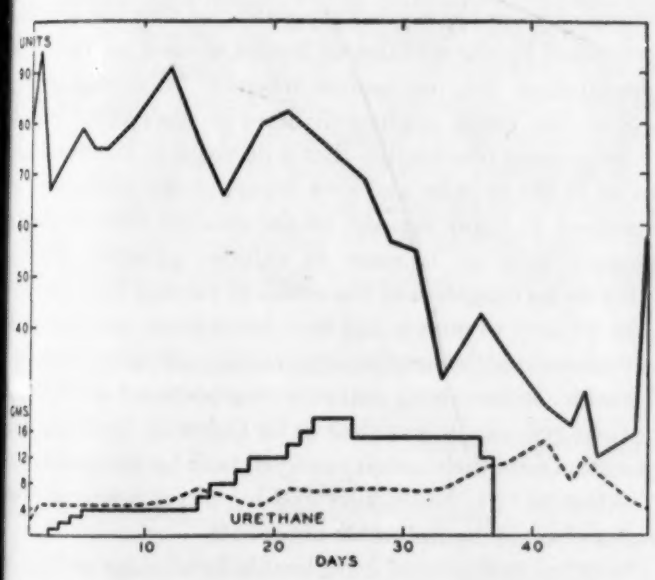



FIG. 1. Changes in acid phosphatase (————) and alkaline phosphatase (----------) of serum induced by toxic amounts of urethane.

cells, while a concentration of 0.002N reduced oxygen consumption about one-half. Ethyl carbamate (*4*) nearly abolished mitosis in the cornea of the rat for brief periods. The present interest in urethane in tumors arose through the work of Haddow and his associates; ethyl and isopropyl phenyl carbamates (*5*) were found to cause a temporary but significant retardation of growth of spontaneous mammary cancer in the mouse and in the Walker carcinoma 256 of rats; in the latter tumor, ethyl carbamate also had an inhibitory effect. Paterson and co-workers (*10*) discovered that ethyl carbamate had a very great palliative effect in human leukemia; there was also some regression in 3 of 13 cases of mammary cancer. Ethyl carbamate in doses of 0.1–1 mg./gram caused a decrease in the leucocyte count in myelogenous leukemia (*2*) in the mouse. Goodman and Lewis (*3*) observed that this agent caused regression of cutaneous metastases of a highly anaplastic carcinoma in one patient; the primary site of the tumor was unknown. We wish to present four observations which prove an effect of ethyl carbamate on prostatic cancer and which deal with its mode of action.

(1) *Ethyl carbamate is a toxic drug which causes inhibition of some cases of prostatic cancer.* In one patient an average daily dose of 9 grams of ethyl carbamate was administered for 33 days with fatal effect. At first there was improvement, with a regression in the size of the prostate, return of sensation in a saddle area of anesthesia due to metastatic involvement of the cauda equina, and a decrease of the acid phosphatase level (Fig. 1) of the blood from 90 to 10 King and Armstrong (*9*) units; however, 6 days after discontinuing the medication, icterus and other evidence of liver damage became evident, and the patient died 6 days later from hepatic necrosis, there being a terminal rise of acid phosphatase. In three patients with wide-spread cancer of the prostate there has been a considerable regression of the primary tumor, relief of pain, an improved sense of well-being, and a significant decrease of the acid phosphatase of the serum (Fig. 2).

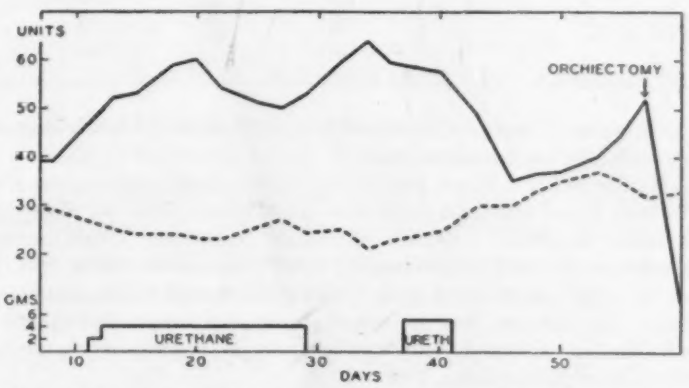



FIG. 2. Decrease in acid phosphatase (————) of serum induced by urethane administration and later by orchiectomy in man. The reciprocal changes in alkaline phosphatase (----------) are indicated.

Effects on the tumor are demonstrable with smaller doses of ethyl carbamate than are required to cause profound changes in the acid phosphatase level where the dosage required approaches the toxic amount. A patient who had an advancing prostatic cancer following a remission induced by orchiectomy, estrogen administration, and roentgenotherapy was found to be bedridden with a large indurated primary tumor and multiple osseous metastasis; 4 grams of ethyl carbamate daily for 5 days, followed by a maintenance dose of 1 gram daily for 6 weeks, eliminated pain and caused great decreases in the size and hardness of the tumor.

Ethyl carbamate must be administered with great caution,

[1] Aided by grants from the Albert and Mary Lasker Foundation, Inc., the Sidney and Frances Brody Foundation, Mr. Ben May, and the Committee for Research in Problems of Sex, National Research Council.

and the leucocyte count of the blood determined frequently. It is not considered safe to continue ethyl carbamate when the leucocyte content is less than 4,000/mm.³ or when nausea and vomiting occur.

(2) *The favorable effects of ethyl carbamate are not due to anti-androgenic action.* The prostatic isolation operation (*8*) was done, and the prostatic secretion collected at 2-day intervals in 3 castrate dogs which received both testosterone propionate (10 mg.) and urethane (4–8 grams) daily for 31 days; the amount of the prostatic secretion increased steadily, proving that the effects of androgen on the prostatic cells were not eliminated.

(3) *Ethyl carbamate does not inhibit glycolysis.* It is well known that tumors are characterized by a high rate of aerobic and anaerobic glycolysis. We have found that urethane in concentrations up to 0.005M had no demonstrable effect on the rate of anaerobic glycolysis in cell-free brain extracts supplemented with glucose and the system described by Utter, Wood, and Reiner (*11*). Lactic acid production was measured manometrically (Table 1). It was concluded that urethane did not inhibit the rate-determining reaction of glycolysis in this particular cell-free system.

TABLE 1

EFFECT OF ETHYL CARBAMATE ON ANAEROBIC GLYCOLYSIS IN RAT BRAIN EXTRACT*

| Exp. | Controls | With ethyl carbamate (0.005M) |
|---|---|---|
| 1 | 99 | 107 |
| | 106 | 103 |
| 2 | 100 | 87 |
| | 87 | 95 |
| 3 | 102 | 100 |
| | 93 | 95 |
| | 104 | 104 |

* Results are expressed in microliters of $CO_2$ liberated in one hour corresponding to lactic acid produced.

Method of Utter, Wood, and Reiner (*11*). The main compartment of the Warburg vessel contained: adenosine triphosphate, 0.0007M; diphosphopyridine nucleotide, 0.0005M; magnesium phosphate, 0.008M; sodium bicarbonate, 0.048M; nicotinamide, 0.04M; phosphate buffer, pH 7.4, 0.01M; 0.05ml. of rat brain extract; and either 0.005M ethyl carbamate or water. The side-arm flask contained glucose and hexose diphosphate to make the final concentration 0.028M and 0.0025M, respectively, in the complete system; final volume, 1 ml.

(4) *Ethyl carbamate has a suppressive effect on the transplantable Sarcoma 39 of rats.* This polymorphous cell sarcoma of albino rats has a 50–90 per cent incidence of takes in our laboratory. The tumor was inoculated subcutaneously in 26 rats, and ethyl carbamate (0.5–1 mg./gm.) was injected daily for 7 days and then at 2-day intervals for 14 days; as a control, 21 rats were inoculated but not injected with urethane. None of the experimental group developed neoplasms, while 12 of the controls grew large tumors. One week after cessation of urethane, 2 of the urethane group developed tumors. Since the dosage of urethane induced anesthesia and weight loss, a further group of controls was established to eliminate the adverse effect of malnutrition on the tumor. Eight rats were inoculated with this tumor and maintained on complete food starvation for 14 days; 4 rats developed tumors on the 9th the 13th day of starvation.

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# Hexokinase Activity and Diabetes Mellitu


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The observations of Price, Cori, and Colowick (*1*) th muscle and liver hexokinase are inhibited, ***in vitro*** by certa fractions of the anterior pituitary gland and that this inhibiti is prevented by the addition of insulin seemed to provide t explanation of the mechanism whereby "diabetogenic" e tracts of this gland produce diabetes in susceptible anima The subsequent observation that a decrease in the hexokina activity of the muscles and liver occurs in the alloxanized r (*2*) seemed to imply support to the concept that diabetes associated with an increase in anterior pituitary activit During an investigation of the action of various tissue extrac on the activity of muscle and liver hexokinase, we have ma observations which question the validity of such a concep

Hexokinase-containing extracts were prepared according t directions generously furnished us by Colowick (personal co munication) and their activity assayed both by the manometr estimation of $CO_2$ production and by direct analysis of th transfer of easily hydrolyzable phosphate.

The extracts displayed considerable hexokinase activity b either manometric or chemical criteria. In confirmation of th results of Price, Cori, and Colowick, it was possible on occasio to demonstrate the inhibition of such activity after addition o the diabetogenic extracts of pituitary and, further to note th reversal of this inhibition after addition of insulin. Of mo than passing interest, however, was the inconstancy of th inhibitory activity of the anterior pituitary extracts. Man apparently identical preparations, known to contain pote diabetogenic factors, failed to produce any inhibition hexokinase activity (Table 1).

Inasmuch as some anterior pituitary extracts known t possess "diabetogenic" activity may fail to inhibit hexokina activity (in crude extracts) while other extracts, prepared i an identical manner, may suppress this activity, it is possib that the anterior pituitary gland may contain an hexokin.s inhibiting factor quite distinct from its "diabetogenic" fact

and that the inconstancy of the demonstration of the inhibiting factor may be a consequence of its extreme lability or poor extraction.

TABLE 1

EFFECT OF "DIABETOGENIC" PITUITARY AND SPLENIC EXTRACTS ON RAT MUSCLE HEXOKINASE ACTIVITY*

| Expt. | Effect of pituitary | $CO_2$ produced (mm.³) | Expt. | Effect of spleen | $CO_2$ produced (mm.³) |
|---|---|---|---|---|---|
| 1 | Extract alone | 53 | 3 | Extract alone | 54 |
| | Extract + APE | 8 | | Extract + 0.4 ml. spleen | 35 |
| | Extract + APE + insulin | 56 | | Extract + 0.4 ml. spleen + insulin | 57 |
| 2 | Extract alone | 48 | | Extract + 0.2 ml. spleen | 46 |
| | Extract + APE | 50 | | Extract + 0.2 ml. spleen + insulin | 53 |
| | Extract + APE + insulin | 50 | | Extract + 0.1 ml. spleen | 49 |
| | | | | Extract + 0.1 ml. spleen + insulin | 53 |

* The hexokinase activity of the muscle extracts was measured manometrically. The APE was prepared according to Young (*3*). The splenic extracts consisted of 1 part spleen + 4 vols. water homogenized in a Waring blendor, adjusted to pH 4, filtered, and the filtrate adjusted to pH 7.5. Insulin was added to a final concentration of 400 γ/ml. Figures give gas production for a 45-minute period of incubation.

Since the results of Price, *et al.* were obtained with fractions of pituitary quite different from those used in the above experiments, our data are not to be construed as a lack of confirmation of their results. They do indicate, however, that a tissue fraction quite distinct from the "diabetogenic" hormone may be responsible for the inhibition of hexokinase activity. That the presence of factors responsible for hexokinase inhibition may not be uniquely confined to the pituitary has been suggested by our observations (Table 1) that splenic extracts actively inhibit hexokinase and that the degree of inhibition

TABLE 2

EFFECT OF INSULIN ON HEXOKINASE EXTRACTS FROM MUSCLES OF ALLOXANIZED AND NORMAL RATS*

| Type of extract | $CO_2$ produced (mm.³) | Micrograms phosphorus/ml. reaction mixture | | | |
|---|---|---|---|---|---|
| | | Before incubation | | After incubation | |
| | | $P_o$ | $P_7$ | $P_o$ | $P_7$ |
| "Alloxanized" extract alone | 60 | 112 | 161 | 109 | 123 |
| Extract + insulin | 59 | 112 | 158 | 111 | 124 |
| "Normal" extract alone | 43 | 87 | 147 | 92 | 118 |
| Extract + insulin | 39 | 87 | 147 | 93 | 117 |

* Muscle extracts were prepared and their hexokinase activity measured manometrically and chemically. The blood sugar of the alloxanized rat was 415 mg. per cent. Results were obtained after a 45-minute incubation. Insulin was added to a final concentration of 400 γ/ml.

is proportional to the amount of splenic extract added. In contrast to the experience of Price, *et al.* with anterior pituitary extracts, the amount of inhibition produced by splenic extracts has been relatively small, due perhaps to their lack of concentration. Whereas splenic extracts almost invariably produce significant inhibition, by manometric criteria, the degree of reversal of this inhibition *in vitro* by added insulin has been most inconstant, varying from no increase in activity to complete restoration. The significance of these observations and the nature of the inhibiting factor are being investigated.

In view of the preceding, we found it pertinent to test the postulate that there is a decrease in the activity of the hexokinase preparations obtained from the muscles and liver of alloxanized rats and that the addition of insulin *in vitro* will cause an increase in the range of normal activities. Rats were rendered diabetic by the administration of alloxan, and extracts of muscles from such rats were prepared as above and used immediately. In all instances, such extracts displayed an hexokinase activity comparable with that found in extracts of normal rat muscles. Further, the addition of insulin failed to increase the activity of either "normal" or "diabetic" extracts (Table 2).

Since our alloxanized rats exhibited a marked hyperglycemia and glycosuria, while the extracts from such rats gave no evidence of a depression of hexokinase activity, it would appear that the disorders of glucose metabolism encountered in diabetes do not necessarily result from any inhibition of hexokinase activity.

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## Antares ($\alpha$ Scorpii)


OTTO STRUVE

*The W. J. McDonald Observatory, Fort Davis, Texas*


The night of July 2–3 was exceptionally fine at the McDonald Observatory, on Mount Locke, in western Texas. The sky was perfectly clear, and the apparent "tremor-discs" of the stars, as seen in the 82-inch reflecting telescope were unusually small. These conditions made it possible for me to carry out an experiment which I had started in the summer of 1940 (*1*), but for the completion of which conditions—atmospheric as well as instrumental—were never sufficiently favorable during the intervening years.

Antares ($\alpha$ Scorpii) is a visual double star, consisting of a first-magnitude, red supergiant and a sixth-magnitude, blue, underluminous helium star. The separation between the two stellar components is 3″ (seconds of arc). Ten years ago O. C. Wilson and R. F. Sanford (*2*) found, at the Mount Wilson Observatory, that the spectrum of the faint blue companion of Antares contains emission lines which correspond to low-level forbidden transitions of ionized iron, [Fe II]. These lines were first identified by Merrill in the spectrum of $\eta$ Carinae, soon after the solution of the problem of the nebular forbidden radiations by Bowen.

The purpose of my work at the McDonald Observatory was to find the source of the forbidden iron lines in the spectrum of the companion of Antares. Good "seeing" conditions were required in order to separate the light of the very luminous red star from that of the faint blue star. I at first turned the large stellar slit-spectrograph (attached below the

Cassegrain focus of the 82-inch telescope) until the slit was at right angles to the line joining the two stars. An exposure of 26 minutes, during which the faint star was kept trailing along 2 mm. of slit length, produced the usual widened spectrum of the helium star, with the lines of [Fe II] in emission superposed over the continuous spectrum. Next, an exposure of 5 minutes, with the star held stationary on the same place upon the slit produced a heavily overexposed continuous spectrum of the star, 0.18 mm. in width, which corresponds to 2.6″ (seconds of arc). This width is due partly to the tremor-disc of the star and partly to photographic overexposure. The forbidden iron lines, expecially λ4287.41, extend on both sides of the star's continuous spectrum, like two little black arrows, to a distance of 0.074 mm., or 1.1″. The appearance of these arrow-like extensions is very much like that of the hydrogen lines in W. W. Campbell's famous "hydrogen-envelope star," and the explanation of the phenomenon is doubtless the same: the [Fe II] emission lines originate in a small nebulosity surrounding the blue companion of Antares.

But before we can be entirely certain we must convince ourselves that the extensions of the emission lines are not a photographic effect. Perhaps the star image was not as tranquil on the slit as I thought, so that underexposed edges on both sides of the heavily exposed strip might leave the continuous star spectrum invisible, though the bright lines would show upon development. To test this I obtained, under similar conditions, with the star-image fixed upon the slit, exposures of 5, 15, and 45 seconds. If the "spilled-over-the-edge" star light had caused the emission lines on the 5-minute exposure, then these short exposures should give the emission lines an opportunity for appearing in the central strip, where the continuous spectrum had appeared on the longer exposure. In reality, the 5-second exposure shows only the barest trace of continuous spectrum; the 45-second exposure shows it plainly. But not one of the three shows even a trace of the [Fe II] lines. The light of the helium star itself does not contain forbidden iron. The emission lines come only from a small nebulosity, about 5″ (seconds of arc) in diameter, which surrounds the helium star.

Next, I turned the spectrograph until the slit was along the line joining the two stars. With two exposures, of 1 and 3 minutes, I could separate completely the two star spectra. The [Fe II] lines again appear as faint extensions on both sides of the helium star. They are not strengthened in the space between the two stars, and, if anything, they suggest that the nebulosity may be slightly elongated in a direction at right angles to the line joining the two stars.

The nebulosity is enormously large in linear measure. The bright red primary star is one of the few whose diameters have been measured by Pease with the Mount Wilson interferometer. It is 0″.040, or 450 times the diameter of the sun. The nebulosity is about 150 times larger, which would make it 50,000 times larger than the sun. The diameter of the helium star has not been measured, but it can be inferred from the temperature and distance to be roughly one or two times the diameter of the sun. Near the outer boundary of the nebulosity the density of the helium star's radiation is weakened by a factor of the order of $10^{-9}$, as compared to the density of radiation within its atmosphere proper. Very roughly, we may say that the nebulosity is about 10 times larger, in diameter, than the solar system.

Despite the fact that from a representative point within the nebula the red star appears as a disc which is about 200 times larger than the blue star, it is the light of the latter—in the ultraviolet region—which is responsible for the ionization of the gases, though not necessarily for the excitation to low-lying atomic levels.

A very strange result of observation is the absence of any other emission lines than [Fe II]. That the permitted Fe II lines are not photographed was explained some years ago by Swings and me as a consequence of what may be described as a fictitiously low excitation temperature. But why are the lines of hydrogen absent? Normally, we observe them with great strength in nebulae, in the interstellar gas, and in almost all star spectra. If they are absent in the nebulosity of Antares, we immediately try to infer that there is too little ionization for recombinations to take place. But since we observe not Fe I (or any other atoms of low ionization potential) in the nebula, we must have a majority of the iron atoms once ionized. The potential is 7.8 volts. Then, if we apply this to hydrogen, with 13.5 volts, we find that approximately 1 out of 10 hydrogen atoms is ionized and therefore capable of producing an emission spectrum by recombination. The usual cosmical abundance of hydrogen is perhaps $10^4$ times greater than that of iron. Hence, there would be all reason to expect the Balmer lines to appear strong in emission (as, in fact, they do in ordinary gaseous nebulae).

It seems to me that the absence of H suggests a real—not only an apparent—paucity of hydrogen in the nebula of Antares. How can we explain this?[1] An attractive idea is to suppose that the nebulosity[2] is not strictly gaseous but that it consists of solid, perhaps even meteoric, particles which have long ago lost most of their hydrogen and are rich in iron. We certainly have such a nebulosity in the solar system, where it leads to the phenomenon of the solar corona on one side and to that of the zodiacal light on the other. We observe emission lines in the corona, but not in the zodiacal light. But that may be due to the relative weakness of the solar radiation in ultraviolet wave lengths. What I am suggesting here is that the [Fe II] radiations in Antares are, in a sense, a counterpart to what in the solar system we know as comet radiations. This hypothesis would explain not only the absence of H but also the very strange dependence upon excitation potential[3] which Swings and I observed in the intensities of permitted Fe II in other, similar objects (WY Geminorum, Boss 1985, etc.).

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[1] We might think of the atmosphere of the earth, which is also poor in H, but which shows, in the spectrum of the night sky, strong forbidden lines of oxygen, [O I]. Since these lines are absent in Antares, as are also the lines of [O II], we must look for a source which is not only depleted in hydrogen (as is the atmosphere of the earth) but also in oxygen and nitrogen—that is, in all light elements.

[2] Astronomers will recall that in 1936 we found a large reddish nebulosity around Antares which shines by reflected light from the red supergiant. This reflection nebula (*Astrophys. J.*, 1936, **84**, 219) is vastly larger than the nebula considered here. There may be no connection between the two, although the large reflection nebula also consists of solid interstellar particles.

[3] An interesting and perhaps significant feature is the great strength, on my recent spectrograms, of [Fe II] 4287, as compared with [Fe II] 4244. They belong to different multiplets.

# IN THE LABORATORY

## An Instrument for Plotting $ED_{50}$ Curves

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Several methods for plotting $ED_{50}$ curves have been described. De Beer (*2*) employed a permanent board with several instruments which enabled him to plot the curve and compute the results accurately and rapidly. Litchfield and Fertig (*3*) have described a rapid and accurate method for the calculation of the $ED_{50}$ value, as have Miller and Tainter (*4*), who employed a special probit paper. Many investigators have used all of these methods, but thus far no instrument has been described which would allow a choice of the method to be used. The instrument described below has been used in our laboratories for over a year and has given accurate results with any of the above methods as well as with the longer Bliss (*1*) method.

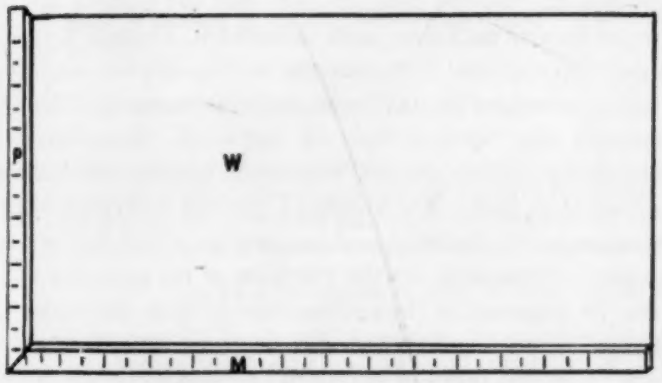


FIG. 1. Completed instruments. P = probit or per cent response scale; M = millimeter graph paper scale; W = Winthrop Probit Paper on plywood base.

The instrument (Fig. 1) was constructed from a piece of plywood 15 x 12 x ¼ inches, bordered by two pieces of molding 1 x ¼ x 15 inches and 12 inches respectively. To the plywood was glued a piece of Winthrop Probit Paper.[1] To the left-hand molding was attached the two scales cut from another piece of the same paper. While being glued, these scales were aligned so that part of the scale extended over the inner edge of the molding and fitted flush with the plywood. Attached to the lower molding was a piece of millimeter graph paper, which was divided into an arbitary scale allowing the plotting of log doses to 3 or more places, depending upon the accuracy desired. The entire board, including scales, was painted with a solution of cellulose nitrate in acetone to protect it against wear.

For plotting the $ED_{50}$ of estrogenic response, where there is a definite logarithmic ratio between each dose, the scales on the plywood are used. The board is covered with a piece of tracing paper, and each dose response is marked off. The provisional and corrected curves relating log dose to probit or per cent response are obtained in the conventional manner, depending upon the method used. In plotting $LD_{50}$ data, the scales on the plywood base of the board are covered with a piece of blank paper, the scales on the molding being used to obtain the dose-response curve. The log-dose values on the horizontal scale are chosen so that the greatest spread between doses will be obtained. This has a tendency to flatten the curve and make the results more accurate. The calculations for the provisional and corrected curves are done in the manner described by the method used.

[1] Obtained from the Winthrop Chemical Company, Rensselaer, New York.

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## Conversion of Heart Potentials Into Auditory Equivalents

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For purposes of our research, it became desirable to have an instrument that would convert to auditory equivalents the changes in electrical potential occurring during the cardiac cycle. In consulting the literature, we found many instruments that involve the simple electronic amplification of the heart sounds (which may then be recorded graphically or phonographically) or the graphic or oscillographic recording of the changes in heart potential: amplifying stethoscopes, recording stethoscopes, stethographs, and electrocardiographs; but we were unable to find what we have termed an electrocardiophone or EKP: an instrument that, instead of expressing the heart potentials in graphic form, expresses them in auditory equivalents.

In developing a frequency modulation amplifier suitable for our purposes, preliminary difficulties were met in handling the extremely low frequencies without distortion. These difficulties have been largely overcome, although alternating-current fields and similar electrical conditions must be avoided.

The basic circuit of the electrocardiophone utilizes the fact that two radio frequencies will produce a beat frequency when fed into a suitable detector circuit. Since the beat frequency is equal to the difference between the frequency of oscillator I and oscillator II, it will be an audible frequency if the oscillators are within a few kilocycles of each other.

Oscillator II (Fig. 1) is adjusted to produce an audible beat note suitable to the operator. The frequency of oscillator I is changed by the reactance tube modulator in accordance with the changes in heart potential, which are amplified by the low-frequency amplifier to a level necessary to actuate the reactance tube modulator.

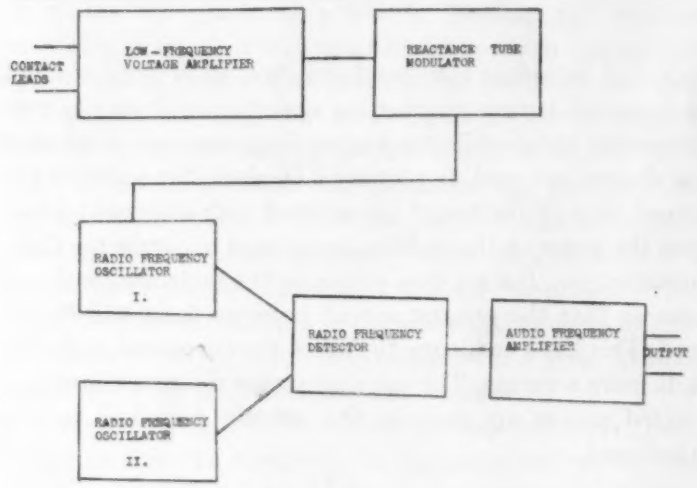


FIG. 1

The output of the detector is also amplified. Although a loud-speaker may be used, we have employed a button earphone so arranged (Fig. 2) that the sounds are conducted by rubber tubing into a standard stethoscope equipped with the conventional chestpiece. The auditory equivalents of the electrical potential changes may thus be cut into the normal stethoscopic sounds, which are not amplified or otherwise distorted. Although no attempt has been made to standardize on any given audio frequency, it is obvious that the heart can "play its piece" on any audible range of frequency—often with interesting effects.

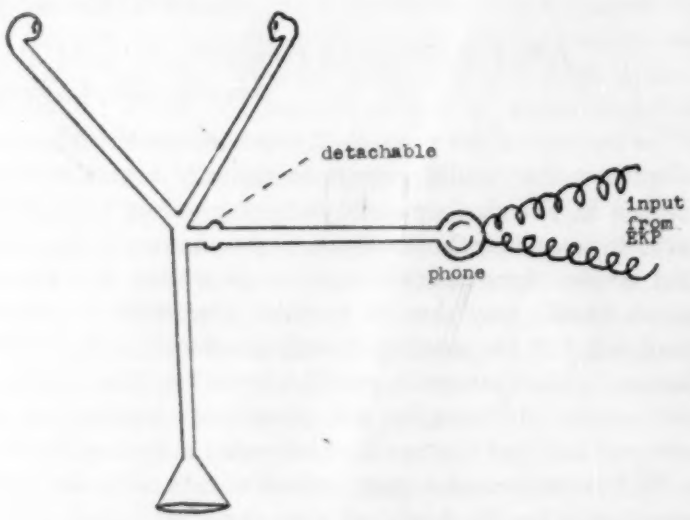


FIG. 2

Correlation of the electrical potential sounds with stethoscopic sounds in health and disease is now being attempted. Further correlation with the electrocardiogram will be tried by the use of a cathode-ray oscilloscope parallel with the electrocardiophone. Sound recordings of both the auditory equivalents of the electrical potential changes and the stethoscopic sounds will permit a more careful dissection of the interrelationship between the heart beat and the potential changes.

The technic should be distinguished from the simple amplification of the changes in heart potential *per se*: these changes are heard only as a clicking sound. For teaching purposes it is held undesirable to use electronic stethoscopic amplification since the resulting sounds depart in quality from those heard with the clinical stethoscope. Since the electrocardiophone utilizes a virgin medium, there is no such conflict here.

The technological details of the apparatus will be published elsewhere.

## Simple Formulas for Calculating Percentage Potency in Three- and Four-Dose Assay Procedures

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In many instances in which the log dose-response curves of unknown and standard substances are parallel straight lines simple formulas for the rapid calculation of the percentage potency of the unknown in terms of the standard are helpful. However, in order to make use of such formulas, it is essential that the assay be so designed that the unknown and standard materials are treated uniformly, *i.e.* the geometric relationship between the individual doses or concentrations of the unknown and standard must be identical, the same diluent must be employed for each, an equal number of dose or concentration levels of each reactant must be used, and the number of replicates per level of each dose must be uniform. Though the actual number of replicates is immaterial to the application of the formulas presented in this paper, it is recommended that, for accuracy's sake, three or four be employed. Moreover, since the formulas in their simplest expression give no indication of the error of an assay, it is suggested that the individual worker determine (a) the limits of accuracy within which the log dose-response is linear and (b) the precision of his proposed assay, so that he is assured of the applicability of these shortcuts.

Formulas for calculating the potency are available when two similarly related doses of standard and unknown are utilized in assay procedures (*5*). The writer is not aware of any such simple formulas for the calculation of the activity in so-called three- or four-dose assay techniques. The desirability of employing more than two logarithmically related doses is apparent if one makes use of graphic representations of data. Obviously, a straight line is the only curve which can be drawn from the data available when only two doses each of standard and unknown are employed. If three or four doses are used, deviations in the linearity of the log dose-response curve become apparent. Moreover, the supplementary data obtained at additional dose levels with little extra work permits the determination of the individual regression lines or, in the case of the four-dose assay, the omission of data at the highest or lowest dose level of the unknown if such data lie outside the limits of linearity of the dose-response curve.

During the development of a thin filter paper disc-agar plate method for the assay of amylases in which the initial concentration of the standard and unknown enzyme extracts was 1 per cent and the three succeeding doses of each were decreased in a 1:5 ratio, a simple formula for calculating the percentage potency of so-called four-dose assays was developed. This formula, which has universal applicability to four-dose assays

der the restrictions given, may be expressed in its simplest rm as follows:

$$\% \text{ Potency} = \text{Antilog}\left[2 \pm c + 5d\,\frac{(U_1 + U_2 + U_3 + U_4) - (S_1 + S_2 + S_3 + S_4)}{[3(U_4 + S_4) + (U_3 + S_3)] - [3(U_1 + S_1) + (U_2 + S_2)]}\right].^{1}$$

this formula, 2 = log 100, the factor for converting the ratio btained to per cent potency; c = the positive expression of e log ratio between the corresponding doses, *i.e.* $U_4$ and $S_4$, the unknown and standard. (In the formula, the sign of c is sitive if the initial dose of the standard was greater, and, nversely, is negative if the initial dose of the standard was naller, than that of the unknown); 5 = the constant for the ur-dose assay; d = the logarithm of the successive dose inrvals of both the standard and the unknown; and $U_1$, $U_2$, $U_3$, $S_1$, $S_2$, $S_3$, and $S_4$ = the sums of the individual responses of e unknown and standard, respectively, for each dose level, ading from the lowest to the highest.

In a similar manner, a formula was developed which is uniersally applicable to three-dose assays performed under the me restricted design. This formula in its broadest, but simlest, expression is as follows:

$$\% \text{ Potency of unknown} = \text{Antilog}\left[2 \pm c + \tfrac{4}{3}d\,\frac{(U_1 + U_2 + U_3) - (S_1 + S_2 + S_3)}{(U_3 + S_3) - (U_1 + S_1)}\right].$$

The terms in this equation have the same meaning as those in the four-dose assay, with the exception that the constant for the three-dose assay is $\frac{4}{3}$ instead of 5.

These formulas, under the restrictions of the test, have universal applicability to any assay in which the log dose-response curve has been shown to be a straight line and the curves of the unknown and standard are parallel. Graphs of the sums of the response at each dose level of both the standard and the unknown reactants give evidence of the parallism of their dose-response curves. If parallelism is not evident, the analysis of variance (*2*), factorial analysis (*3*), and the determination of lambda (*1*) may be necessary to interpret the significance of the assay. Any person familar with factorial analysis will recognize the numerators of the fractions given as the sum of the products dealing with the difference between samples, and the denominators as the sum of the products dealing with the slope of the dosage-response curve, *i.e.* S(xYp), which were given by Bliss and Marks in their factorial scheme for three- and four-dose assays (*3*). The application of the formulas presented here is, however, simpler than that of the potency formula given by these authors, *i.e.* $M = \frac{kID}{B}$. Moreover, both types of formulas give the same potency.[2]

These formulas have been applied in the Wellcome Laboratories to such widely divergent types of assay as agar diffusion methods for determining the potency of antibiotics or of amylases, turbidimetric procedures of assaying for a pneumococcus growth factor, and the mouse squeak test for the assay of analgesics. In the opinion of the author, a four-dose assay is preferable, since it permits the omission of the data from a single dose level (whether high or low), if the limit of linearity of the dose-response curve has been exceeded with the unknown. Hence, calculation of the potency on the basis of the three remaining dose levels may be made by applying the formula for the three-dose assay.

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[1] The formula is derived in the following manner from the original Gaddum formula (*4*), *i.e.*

$$\text{log ratio of potencies} = \frac{\bar{y}_U - \bar{y}_S}{b} - (\bar{x}_U - \bar{x}_S),$$

where $\bar{y}_U$ = mean response of the unknown, $\bar{y}_s$ = mean response of the standard, b = combined slope of the dosage-response curves of the unknown and standard preparations, $\bar{x}_U$ = mean log dose of the unknown, and $\bar{x}_S$ = mean log dose of the standard. But the mean response of the unknown = $\frac{(U_1 + U_2 + U_3 + U_4)}{4N}$, where 4 = the number of doses, N = the number of replicates per dose, and $U_1$, $U_2$, $U_3$, and $U_4$ represent the sums of the replicates for each successive dose grading from the lowest to the highest; similarly, the mean response of the standard is $\frac{(S_1 + S_2 + S_3 + S_4)}{4N}$. Moreover, where X = the individual polynomial coefficients of the linear term and d = log dose interval, the slope of the unknown, *i.e.* $b = \frac{2S(xYp)}{dNS(X^2)}$ becomes $\frac{2(3U_4 + U_3 - U_2 - 3U_1)}{dNS(X^2)}$ and that of the standard, $\frac{2(3S_4 + S_3 - S_2 - 3S_1)}{dNS(X^2)}$.

Hence, the average slope of the unknown and the standard is

$$\tfrac{1}{2}\left[\frac{2(3U_4 + U_3 - U_2 - 3U_1 + 3S_4 + S_3 - S_2 - 3S_1)}{dNS(X^2)}\right].$$

But $X^2 = 20$ for a four-dose assay. Therefore, by substituting and combining terms, the average slope becomes

$$\frac{[3(U_4 + S_4) + (U_3 + S_3)] - [3(U_1 + S_1) + (U_2 + S_2)]}{20\,dN}.$$

By further substituting in the Gaddum formula, the following result is obtained: the ratio of potency of unknown to standard = $\frac{(U_1 + U_2 + U_3 + U_4) - (S_1 + S_2 + S_3 + S_4)}{4N} \cdot \frac{20\,dN}{[3(U_4 + S_4) + (U_3 + S_3)] - [3(U_1 + S_1) + (U_2 + S_2)]}$ + $(\bar{x}_S - \bar{x}_U)$; this reduces to the formula in the text, since $c = \bar{x}_S - \bar{x}_U$.

[2] After this paper was in press, it was suggested to the author that, for convenience, the formula for the two-dose assay should be included. In order to make the previous formula analogous to the formulas herein presented the term c has been included, and the terms in its denominator have been rearranged. The revised formula for the potency of the unknown in a two-dose assay procedure is as follows:

$$\% \text{ Potency} = \text{Antilog } 2 \pm c + d\,\frac{(U_2 + U_1) - (S_2 + S_1)}{(U_2 + S_2) - (U_1 + S_1)}$$

# Book Reviews

***Retinal structure and colour vision: a restatement and an hypothesis***. E. N. Willmer. Cambridge, Engl.: at the Univ. Press, 1946. Pp. xii + 231. (Illustrated.) $4.50.

This book is essentially the statement of an hypothesis of color vision. It contains a Foreword, a Preface, seven chapters, and an Addendum. The Foreword, by W. D. Wright, recommends the book with obvious misgivings. The Preface, by the author, tells us that what follows is "frankly provocative and speculative." And so, indeed, it is.

The first chapter is mainly histological description of the retinal elements, including not only the rods and cones, but the neural elements as well. The second chapter, which treats of the functions of the retinal elements, presents information about nerve impulses, dark adaptation, the spectral sensibilities of the rods and cones, and about visual purple and visual violet.

With the third chapter the presentation of the hypothesis begins and is continued through the next three chapters. The seventh chapter deals with color blindness and with the bearing of Willmer's hypothesis on it.

The Addendum, written after the rest of the book was in press, records some recent experiments on color vision of the fovea and further elaborates the hypothesis. It closes with a general statement of the ideas involved. A list of references and two indexes follow.

The essential thesis of this book rests on the fact that only two receptors—rods and cones—can be differentiated histologically in the retina. The author then assumes that color vision depends on the combined action of these two receptors. The rods are mainly concerned with the short-wave or blue and green end of the spectrum; the cones, with the long-wave or yellow and red end of the spectrum. The various color sensations result from the relative stimulation of the two receptor systems by the different parts of the spectrum.

The main quantitative prop for this novel idea comes from manipulation of the spectrum luminosity curves of the rods and cones when these are of equal height or equal area. If for each wave length one plots the cone luminosity as abscissa and the rod luminosity as ordinate, the resulting curve roughly resembles the standard international (ICI) spectrum locus plotted on a right triangle. Some additional assumptions and a logarithmic plot of the cone and rod luminosities for each wave length result in a diagram which vaguely resembles the just discriminable chromaticity step data developed by MacAdam and by Wright for the color domain. A further translation from luminosity to frequency of nerve impulses in rod and cone fibers yields curves which describe in a roughly quantitative way the saturation of the spectrum and the addition of white to spectral colors.

Finally, since one of the central facts of color vision is its trichromatic nature, a third receptor is added to the rods and cones. This is a hypothetical non-dark-adapting day-rod whose properties are not defined too clearly, but whose spectral sensibility may be different from that of ordinary rods. The fovea centralis is described as composed of cones and of these non-adapting day-rods, which makes it dichromatic, as some experiments appear to show.

All this is amusing and speculative, and would have made an interesting afternoon's conversation between the enthusiastic author and a more critical mentor. Presented as a book of over 200 pages, however, the idea becomes labored and unconvincing. Its central thesis rests on a misconception. The rod and cone luminosity curves are usually drawn to equal heights for convenience, not because they are really so. Actually the rod maximum is about 50 times as high as the cone maximum. Moreover, while some observers have a few rods in the fovea, many people show none. Still, color vision is essentially a phenomenon of the fovea.

The audience of this perverse book is a limited one, because only those who are thoroughly familiar with the data of vision in general and of color vision in particular can read it with the necessary critical evaluation. Others will surely become confused, not only because of the strange and incomplete nature of the ideas, but because of the mistakes and misunderstandings, of which there are many.

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***Statistical analysis in biology***. (2nd ed.) K. Mather. New York: Interscience, 1947. Pp. 267. $5.00.

Because of its clarity, the first edition of this book gained considerable favor among biologists. The revised second edition is changed in no fundamental respect. It includes a new chapter on the angular transformation for proportions and the probit transformation for dosage-response data, written in the same clear style. Other changes involve the addition of footnotes, corrections of typographical errors, and new dating of references.

The book covers the common tests of significance, the normal deviate test, the t-test, the $X^2$-test, and the analysis of variance F-test, exhibiting their use in a considerable variety of biological experiments. The mathematical models of frequency distributions which arise most often in practice are explained rather thoroughly. These include the binomial, the normal, and the Poisson distributions. Three chapters on two or more variates and a chapter on estimation of unknown parameters complete the volume.

The author has placed emphasis on the advantages of planning experiments in order to extract maximum information from the observations. More emphasis might be placed upon the principles and methods of estimation, carrying the exposition of these methods along with the discussion of tests of significance rather than relegating them to a late chapter. An introduction to the concepts of the power of a statistical test and of errors of the first and second kind in testing statistical hypotheses might not be amiss in a volume of this sort, although an exposition for students in the nonmathematical sciences might present a considerable problem.

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